10/755,889

```
=> d his

     (FILE 'HOME' ENTERED AT 15:00:23 ON 29 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 15:00:55 ON 29 JAN 2007
L1          3538 S BCL-6
L2          3466 S "NFKB"
L3             0 S L1 AND L2
L4           265 S LAZ3 OR "ZINC FINGER PROTEIN 51"
L5             0 S L2 AND L4
L6         49561 S "B CELL CLL" OR "B CELL LYMPHOMA"
L7            24 S L6 AND L2
L8            22 DUP REM L7 (2 DUPLICATES REMOVED)
                 E NADLER S G/AU
L9           177 S E3
                 E NEUBAUER M G/AU
L10           74 S E3
                 E FEDER J N/AU
L11          190 S E3
                 E CARMAN J/AU
L12          105 S E3
L13          538 S L9 OR L10 OR L11 OR L12
L14            0 S L13 AND L8
L15            4 S L13 AND L2
L16            4 DUP REM L15 (0 DUPLICATES REMOVED)

=>
```

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1652mxm

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS	4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS	5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS	6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS	7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS	8	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS	9	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS	10	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS	11	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS	12	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS	13	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS	14	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS	15	DEC 18	CA/CAplus patent kind codes updated
NEWS	16	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS	17	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	18	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS	19	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	20	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS	21	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	22	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	23	JAN 22	CA/CAplus updated with revised CAS roles
NEWS	24	JAN 22	CA/CAplus enhanced with patent applications from India

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:00:23 ON 29 JAN 2007

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 15:00:55 ON 29 JAN 2007

FILE 'EMBASE' ENTERED AT 15:00:55 ON 29 JAN 2007
Copyright (c) 2007 Elsevier B.V. All rights reserved.

FILE 'BIOSIS' ENTERED AT 15:00:55 ON 29 JAN 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'BIOTECHDS' ENTERED AT 15:00:55 ON 29 JAN 2007
COPYRIGHT (C) 2007 THE THOMSON CORPORATION

FILE 'SCISEARCH' ENTERED AT 15:00:55 ON 29 JAN 2007
Copyright (c) 2007 The Thomson Corporation

FILE 'HCAPLUS' ENTERED AT 15:00:55 ON 29 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'NTIS' ENTERED AT 15:00:55 ON 29 JAN 2007
Compiled and distributed by the NTIS, U.S. Department of Commerce.
It contains copyrighted material.
All rights reserved. (2007)

FILE 'LIFESCI' ENTERED AT 15:00:55 ON 29 JAN 2007
COPYRIGHT (C) 2007 Cambridge Scientific Abstracts (CSA)

=> s bcl-6
L1 3538 BCL-6

=> s "nfkb"
L2 3466 "NFKB"

=> s l1 and l2
L3 0 L1 AND L2

=> s laz3 or "zinc finger protein 51"
L4 265 LAZ3 OR "ZINC FINGER PROTEIN 51"

=> s l2 and l4
L5 0 L2 AND L4

=> s "b cell cll" or "b cell lymphoma"
6 FILES SEARCHED...
L6 49561 "B CELL CLL" OR "B CELL LYMPHOMA"

=> s l6 and l2
L7 24 L6 AND L2

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8 22 DUP REM L7 (2 DUPLICATES REMOVED)

=> d 1-22 ibib ab

L8 ANSWER 1 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1312634 HCAPLUS
DOCUMENT NUMBER: 146:56479
TITLE: Method of profiling a CD133+ and/or CD34+ cell population from human cord blood and related sialylated N-glycan cell surface markers and mRNA markers for related glycoproteins and/or glycosynthase proteins
INVENTOR(S): Jaatinen, Taina; Hemmoranta, Heidi; Partanen, Jukka; Laine, Jarmo; Satomaa, Tero; Natunen, Jari; Blomqvist, Maria
PATENT ASSIGNEE(S): Suomen Punainen Risti, Veripalvelu, Finland; Glykos Finland Oy
SOURCE: PCT Int. Appl., 215pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006131599	A2	20061214	WO 2006-FI50237	20060606

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: FI 2005-5291 A 20050606
FI 2005-5464 A 20050831
FI 2006-206 A 20060301

AB The present invention relates to a method of profiling a cell population comprising a step of detecting the presence or absence of at least two biol. markers in said cell population, wherein at least one of said markers is a cell surface marker, which is a sialylated N-glycan marker with structure NeuNAcα3Gal, and at least one of said markers is a mRNA marker related to glycoproteins and/or glycosynthase proteins. The invention also relates to method for purification of cord blood cell population and to a complete cell population from cord blood purified by said method.

L8 ANSWER 2 OF 22 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
DUPLICATE 1
ACCESSION NUMBER: 2005-26503 BIOTECHDS
TITLE: New isolated nucleic acid having a promoter comprising a cell cycle-specific regulatory region, a cell type-specific enhancer, and encoding a therapeutic, for treating hyperproliferative diseases;
the use of a virus toxin, an immunostimulant and RNA interference for a gene therapy application
AUTHOR: HUI K M; HO A I; LAM Y P P
PATENT ASSIGNEE: HUI K M
PATENT INFO: WO 2005085455 15 Sep 2005
APPLICATION INFO: WO 2005-SG75 9 Mar 2005
PRIORITY INFO: AU 2004-901220 9 Mar 2004; AU 2004-901220 9 Mar 2004

DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2005-630731 [64]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule comprising a promoter comprising a cell cycle-specific regulatory region, a cell type-specific enhancer element, and a sequence encoding a therapeutic agent operably linked to the promoter, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated vector comprising the new nucleic acid molecule; and (2) treating a hyperproliferative disease or disorder in a subject, comprising administering to the subject, the vector of (1) and treating the hyperproliferative disease or disorder.

BIOTECHNOLOGY - Preferred Nucleic Acid: The cell specificity of the isolated nucleic acid molecule is conferred by a glial cell specific element, and confined by a cell cycle-dependent element. The therapeutic gene encodes a cell toxic agent, RNAi or an immune enhancer. The toxic agent is derived from a plant, fungus, animal or a synthetic chemical library, particularly from a plant or fungus selected from Amanita Verna (a basidiomycyte), Phaseolus vulgaris, Arbus precatorius, Robinia pseudoacacacia, Aleurites fordii, Ricinus comunis, Viscum album, Phoradendron serotinum, Penicillium conidophores, Synsephalum dulciferum, Zizyphus obtusifolius, lecithinase (phospholipase C), alpha-, beta-, gamma-, delta-toxins of staphylococci, streptococcal streptolysins, cholera toxin, pertussis toxin, Escherichia coli LT toxin, tetanus toxin, botulin toxin, sialidase, Bacillus anthracis, pertussis toxin, alpha-, beta-, epsilon-, tau-, and theta- toxins of clostridium. The therapeutic gene also induces a physiological effect selected from apoptosis, an enhanced immune response, a cellular growth-retardation response and a modulation of gene expression response, and is apoptosis-associated tyrosine kinase, apoptotic protease activating factor, baculoviral IAP repeat-containing 2, baculoviral IAP repeat-containing 3, baculoviral IAP repeat-containing 4, baculoviral IAP repeat-containing 5 (survivin), baculoviral IAP repeat-containing 6, apoptosis inhibitor 5, BCL-2-antagonist of cell death, BCL-2-antagonist/killer 1, BCL-2-associated X protein, B-cell CLL /lymphoma 2, B-cell CLL/lymphoma 10, BH3 interacting domain death agonist, BCL-2-interacting killer (apoptosis-inducing), BCL-2-related ovarian killer, CASP8 and FADD-like apoptosis regulator, cell death-inducing DFFA-like effector a, CASP2 and RIPK1 domain containing adaptor with death domain, defender against cell death 1, death-associated protein, death associated protein 3, death-associated protein kinase 1, death-associated protein kinase 3, death-associated protein 6, eukaryotic translation initiation factor 4 gamma, 2, harakiri, BCL-2-interacting protein (contains only BH3 domain), FasL associated via death domain, FADD, baculoviral IAP repeat-containing 1, programmed cell death 1, programmed cell death 2, programmed cell death 8 (apoptosis-inducing factor), receptor (TNFRSF)- interacting serine-threonine kinase 1, receptor-interacting serine-threonine kinase 2, ring finger protein 7, serine/threonine kinase 17a (apoptosis-inducing), serine/threonine kinase 17b (apoptosis-inducing), TRAF family member-associated NFKB activator and TNFRSF1A-associated via death domain. The apoptotic gene is FasL or FADD. The cell-specific enhancer is specific is from a brain cell, a skin cell, a kidney cell, a lung cell, a muscle cell, a blood cell, a kidney cell, a liver cell, a breast cell and a bone cell, and is the glial fibrillary acidic protein (GFAP) enhancer. Preferred Vector: The vector is viral vector selected from papovaviruses, adenoviruses, vaccinia viruses, adeno-associated virus, herpesviruses including HSV and EBV, lenti-viruses and retro viruses, and preferably a HSV-1 amplicon viral. Preferred Method: The vectors are administered to the subject ex vivo, where the cancer cells are removed from a subject, contacted with the vector and then the cancer cells are returned to the subject. The vectors are also administered to the subject in vivo.

ACTIVITY - Cytostatic; Antiarteriosclerotic; Vasotropic; Antipsoriatic; Antiinflammatory; Antiarthritic; Nephrotropic; Gynecological; Immunosuppressive; Ophthalmological; Dermatological; Virucide. No biological data given.

MECHANISM OF ACTION - Gene therapy; Apoptosis inducer.

USE - The vector is useful in the treatment of a hyperproliferative disease or disorder, such as cancer, liver disease including hepatocarcinoma, blood vessel proliferative disorders including restenosis, atherosclerosis, in-stent stenosis, vascular graft restenosis, fibrotic disorders, psoriasis, inflammatory disorders, such as arthritis, glomerular nephritis, endometriosis, macular degenerative disorders, benign growth disorders such as prostate enlargement and lipomas or autoimmune disorders, where the cancer is lung cancer, hepatocellular cancer, lymphoma, pancreatic cancer, stomach cancer, skin cancer, basal cell carcinoma, testicular cancer, ovarian cancer, head and neck cancer, bone cancer, breast cancer, kidney cancer or prostate cancer, squamous cell papilloma, choroid plexus papilloma or laryngeal papilloma, genital warts, plantar warts, epidermodysplasia verruciformis or malignant warts, and preferably brain cancer, such as gliomas, astrocytoma, brain stem glioma, ependymomas, oligodendrogliomas, medulloblastoma, meningioma, schwannomas, craniopharyngiomas, germinoma, pineocytoma, pineoblastoma, neuroblastoma, neurocytoma, ganglioneuroma and oligodendroglioma (all claimed).(89 pages)

L8 ANSWER 3 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1125605 HCAPLUS
DOCUMENT NUMBER: 143:400850
TITLE: Diagnosing depression by analyzing expression profiles of marker genes
INVENTOR(S): Rokutan, Kazuhito; Ohmori, Tetsuro; Morita, Kyoko; Ohta, Masayuki; Saito, Toshiro
PATENT ASSIGNEE(S): Hitachi Ltd., Japan
SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1586657	A1	20051019	EP 2005-6769		20050329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU					
JP 2005312435	A	20051110	JP 2005-42534		20050218
US 2005239110	A1	20051027	US 2005-91674		20050329
PRIORITY APPLN. INFO.:			JP 2004-96068	A	20040329
			JP 2005-42534	A	20050218

AB The present invention relates to a method of diagnosing depression, wherein gene expression is analyzed using mRNA of patients' peripheral bloods to cluster patients afflicted with depression, and conditions thereof are then diagnosed. The present inventors have focused on peripheral leukocytes that can be easily obtained as specimens and allow many receptors of factors associated with stress responses to be expressed therein in order to objectively diagnose the conditions of depression, in the development of which stress plays an important role. They have extensively analyzed the expression patterns of mRNAs of approx. 1,500 genes associated with stress responses and then developed certain patterns. Thus, they have found a method that is capable of classification patients afflicted with depression and diagnosing the conditions thereof. More specifically, the present invention relates to a method of diagnosing depression, wherein gene expression is analyzed using mRNA of a subject's peripheral blood to evaluate whether or not the subject is afflicted with

depression, the type of depression of a subject who had been evaluated as being afflicted with depression is identified, and the conditions of depression are then diagnosed in accordance with the type of depression. According to this method, the expression profiles of the marker gene for depression (an indicator for evaluating whether or not a subject has been afflicted with depression) selected from among the genes listed in Table 1 can be employed to evaluate whether or not a subject is afflicted with depression. When a subject was evaluated as being afflicted with depression, the expression profiles of the marker gene for classification (an indicator for classifying a patient afflicted with depression) selected from among the genes listed in Table 2 can be employed to identify the type of depression in the subject to be type PA or PB. The present inventors extracted RNA from the whole blood collected from patients and healthy volunteers as described below, and gene expression of patients was then analyzed using DNA chips, along with that of healthy volunteers. The marker genes were determined based on the results.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:532674 BIOSIS

DOCUMENT NUMBER: PREV200510326189

TITLE: Latent membrane protein 1 of Epstein-Barr virus affects endogenous signaling pathways in human B cells.

AUTHOR(S): Lambert, Stacie [Reprint Author]; Martinez, Olivia

CORPORATE SOURCE: Stanford Univ, Sch Med, Dept Surg, Div Transplantat,Transplant Immunol Lab, Stanford, CA 94305 USA

SOURCE: FASEB Journal, (MAR 4 2005) Vol. 19, No. 4, Suppl. S, Part 1, pp. A957-A958.
Meeting Info.: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences. San Diego, CA, USA. March 31 -April 06, 2005. Amer Assoc Anatomists; Amer Assoc Immunologists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr Sci; Amer Soc Pharmacol & Expt Therapeut; Int Union Physiol Sci.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 1 Dec 2005
Last Updated on STN: 1 Dec 2005

AB Epstein-Barr virus (EBV) call transform human B cells in culture and is associated with some forms of clinical B cell lymphoma. Oncogenic transformation of cells by EBV requires latent membrane protein I (LMP1), an EBV protein that constitutively signals through cellular TRAF signaling adaptor proteins. TRAF proteins are also involved in normal signaling pathways downstream of most TNF receptor superfamily members. Using paired EBV-negative and EBV-infected Burkitt's lymphoma cells, we found reduced responsiveness of EBV-infected cells to stimulation through TNF receptor superfamily members. EBV-negative B cells werestably transfected with a chimeric triggerable LMP1 construct to test the hypothesis that this is due to the presence of LMP1 signaling. Chimeric LMP1 signals when crosslinked, as confirmed by NFkB reporter activation, IL-10 induction, and ICAM-1 upregulation. LMP1 signaling in transfected B cells as well as in EBV-infected B cells inhibited the association of TRAF signaling adaptor proteins with crosslinked TNFR superfamily members. This data indicates that LMP1signaling may disrupt the normal signaling of TNFR superfarmly members by usurping interactions with TRAFs. We anticipate that investigation of LMP1 signaling effects on endogenous receptor triggered signaling pathways that affect B cell function will result in a greater understanding of how EBV hijacks human B cells. Research support from Stanford Immunology Program Training Grant and American Cancer Society.

L8 ANSWER 5 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:352219 BIOSIS
DOCUMENT NUMBER: PREV200510137925
TITLE: Response of malignant B lymphocytes to ionizing radiation: Gene expression and genotype.
AUTHOR(S): Lyng, Heidi [Reprint Author]; Landsverk, Kirsti S.; Kristiansen, Elin; DeAngelis, Paula M.; Ree, Anne H.; Myklebost, Ola; Hovig, Eivind; Stokke, Trond
CORPORATE SOURCE: Norwegian Radium Hosp, Dept Radiat Biol, N-0310 Oslo, Norway
heidi.lyng@labmed.uio.no
SOURCE: International Journal of Cancer, (JUL 20 2005) Vol. 115, No. 6, pp. 935-942.
CODEN: IJCNAW. ISSN: 0020-7136.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Sep 2005
Last Updated on STN: 8 Sep 2005
AB The human malignant B-lymphocyte cell lines Reh and U698 show arrest in G, phase after ionizing radiation (IR), but only Reh cells arrest in G, phase and die by apoptosis. We have used cDNA microarrays to measure changes in gene expression at 2, 4 and 6 hr after irradiation of Reh and U698 cells with 0.5 and 4 Gy in order to begin exploring the molecular mechanisms underlying the phenotypic changes. We also investigated whether gene expression changes could be caused by possible aberrations of genes, as measured by comparative genomic hybridization. Reh cells showed upregulation of CDKN1A that likely mediated the G, arrest. In contrast, U698 cells have impaired function of TP53 protein and no activation of CLIKN1A, suppressing the arrest in G(1). The G, arrest in both cell lines was likely due to repression of PLK1 and/or CCNF. IR-induced apoptosis in Reh cells was probably mediated by TP53 and CDKN1A, whereas a high expression level of MCL1, caused by gene amplification, and activation of the NFKB pathway may have suppressed the apoptotic response in U698 cells. Genes suggested to be involved in apoptosis Were activated long before this phenotype was detectable and showed the same temporal expression profiles as genes involved in cell cycle arrest. Our results suggest that differences in functionality and/or copy number of several genes involved in IR-regulated pathways contributed to the phenotypic differences between Reh and U698 cells after IR, and that multiple molecular factors control the radiation response of malignant B lymphocytes. (c) 2005 Wilev-Liss, Inc.

L8 ANSWER 6 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:182667 BIOSIS
DOCUMENT NUMBER: PREV200600184779
TITLE: Cell based assays completed with the mantle cell lymphoma cell lines Z138 and NCEB-1 indicate that combinations of bortezomid and flavopiridol interact to achieve synergistic activity.
AUTHOR(S): Kapanen, Anita [Reprint Author]; Tucker, Catherine; Chikh, Ghania; Bally, Marcel; Klasa, Richard
CORPORATE SOURCE: BC Canc Agcy, Dept Adv Therapeut, Vancouver, BC, Canada
SOURCE: Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 678A.
Meeting Info.: 47th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA. December 10 -13, 2005. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Mar 2006
Last Updated on STN: 15 Mar 2006
AB Mantle cell lymphoma (MCL) has the poorest long-term survival of all the

lymphoma subtypes. CHOP-like regimens currently represent the standard of care for individuals with MCL, but traditional chemotherapeutic regimens do not elicit disease free survival times that are comparable to other sub classes of B-cell lymphomas. Median
survival rate of a MCL patient still is approximately 3 years. Therefore new, targeted therapeutics are needed to improve the clinical outcome of MCL. The aim of the study was to identify and characterize combination effects achieved when flavopiridol, a Cyclin D1 inhibitor, and bortezomib, a proteosome inhibitor, are used in a combination setting together or with other agents contained in the CHOP regimen. Two MCL cell lines, Z138 and NCEB-1, were tested for cytotoxicity of drugs alone and in combinations, where alamar blue was used to assess cell viability. The resulting data were analyzed by using the median effect principle introduced by Chou and Talalay. In addition, mechanisms governing measured cytotoxic effects and combination effects were studied by DNA staining (propidium iodine), Caspase 3/7 activation and by western analysis of cyclin1, NfkB, Bcl-xl, Bax and Bcl-2. The combination of bortezmib and flavopiridol was found to be synergistic in both cell lines studied. Synergistic interactions were dependent on drug-to-drug ratio. In NCEB-1, a ratio 1: 12000 (bortezomib:flavopiridol) determined based on the IC90 of each of the individual agents showed synergy over a broad range of fa values (representing the fraction of affected cells). At ratios based on the IC10 and IC50 of the agents when used alone produced effects that were estimated to be antagonistic by the median effect principle. In the Z138 cell line, drug to drug ratios based on the individual agent IC50 and IC90 resulted in synergistic interactions. Consistent with the objective of identifying synergistic combinations, a clear dose reduction was observed to achieve a given therapeutic goal (e.g. 90% cell kill). 10-fold less bortezomib and 55-fold less flavopiridol would be required to achieve 90% cell death/cytostasis based on addition of the agents alone. Mechanistic studies showed that bortezomib in the combination and alone activated the caspase-dependent apoptotic pathway. The combination of bortezomib and flavopirdol for treatment of MCL would appear to an appropriate choice for clinical evaluation, however novel strategies must be developed in order to insure that combination effects observed in cell based screening assays are capture in patients. In this regard it is important to consider drug-drug ratio effects as well as combination engendered toxicities, both parameters that can be evaluated through careful pharmacodynamic assessments in well defined animal models of MCL.

L8 ANSWER 7 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:180866 BIOSIS
DOCUMENT NUMBER: PREV200600182978
TITLE: Signatures of response to the proteasome inhibitor bortezomib in diffuse large B-cell lymphoma.
AUTHOR(S): Feuerhake, Friedrich [Reprint Author]; Monti, Stefano; Blank, Jonathan; Wu, Erxi; Chen, Wen; Golub, Todd R.; Shipp, Margaret A.
CORPORATE SOURCE: Dana Farber Canc Inst, Boston, MA 02115 USA
SOURCE: Blood, (NOV 16 2005) Vol. 106, No. 11, Part 1, pp. 181A. Meeting Info.: 47th Annual Meeting of the American-Society-of-Hematology. Atlanta, GA, USA. December 10 -13, 2005. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Mar 2006
Last Updated on STN: 15 Mar 2006

AB The proteasome inhibitor, bortezomib (VELCADE (R), formerly PS341), has significant anti-tumor activity in several lymphoid malignancies. Reported targets of this broad-based inhibitor include the NFKB pathway (I K B A). Recently defined subtypes of large B-

cell lymphoma (LBCL) exhibit constitutive activation of NFKB, prompting us to analyze the efficacy of bortezomib in a panel of 10 DLBCL cell lines. Six of the diffuse LBCL cell lines were sensitive to bortezomib treatment at doses below 10 nM (range IC50 = 2.9 to 6.9 nM) whereas 4 cell lines were resistant at 10 nM (IC50 = 14.8 to 70.2 nM). Baseline proteasomal function, as defined by cleavage of the 20S proteasome-specific fluorogenic peptide LLVYAMC, was similar in sensitive and resistant DLBCLs; however, the IC50 for bortezomib proteasomal inhibition was somewhat lower in sensitive vs. resistant lines (sens. vs res., p = .04, one-sided t test). Baseline NFKB activity varied widely in the DLBCL cell lines and did not differ in cell lines that were sensitive vs. resistant to bortezomib. Ten nM bortezomib did not inhibit NF K B activity in resistant DLBCL cell lines whereas the same dose reduced NF K B activity in sensitive DLBCL cell lines (sens. vs. res., p < .005, rank test [Mann-Whitney]). However, 5 of 6 sensitive DLBCL cell lines had very low baseline NF K B levels (< 0.5 relative absorbance units) suggesting that NFKB inhibition was not a major factor in bortezomib response and prompting further analysis of additional bortezomib targets. Three sensitive and I resistant DLBCL cell line were selected for detailed analyses of transcriptional profiles following bortezomib treatment. We developed an algorithm for identifying genes that were significantly up- or down-regulated in the bortezomib-sensitive cell lines but unchanged in the resistant line. In addition, we utilized gene set enrichment analysis (GSEA) and gene ontogeny (GO) termed enrichment to interpret the molecular signatures of response. Genes down-regulated in response to bortezomib included critical B-cell transcription factors, components of the B-cell receptor signaling cascade and genes regulating mitosis and cell cycle control; up-regulated genes included heat shock proteins (HSP) and multiple proteasomal components. Consistent with the functional data, downregulation of NF K B target genes was not a common feature in all bortezomib-sensitive cell lines. In contrast, target genes of the c-MYC transcription factor were significantly down-regulated and c-MYC activity was decreased in sensitive (but not resistant) DLBCL cell lines following bortezomib treatment (sens. vs. res., p < .005, rank test). Taken together, the results provide insights into likely mechanisms of action of bortezomib in DLBCL, highlighting c-MYC as a potentially important target and identifying HSP as a complementary target to overcome bonezomib resistance.

L8 ANSWER 8 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:346344 BIOSIS
DOCUMENT NUMBER: PREV200400345096
TITLE: High-throughput retroviral tagging for identification of genes involved in initiation and progression of mouse splenic marginal zone lymphomas.
AUTHOR(S): Shin, Min Sun; Fredrickson, Torgny N.; Hartley, Janet W.; Suzuki, Takeshi; Agaki, Keiko; Morse, Herbert C. III [Reprint Author]
CORPORATE SOURCE: Immunol LabNIH, NIAID, 5640 Fishers Lane, Rockville, MD, 20852, USA
hmorse@niaid.nih.gov
SOURCE: Cancer Research, (July 1 2004) Vol. 64, No. 13, pp. 4419-4427. print.
ISSN: 0008-5472 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Aug 2004
Last Updated on STN: 18 Aug 2004

AB Human B-cell lymphomas are frequently associated with specific genetic changes caused by chromosomal translocations that activate protooncogenes. For lymphomas of mice expressing murine leukemia virus, mutagenic proviral insertions are thought to play a similar role. Here we report studies designed to

determine whether specific retroviral integration sites might be associated with a specific subset of mouse B-cell lymphomas and if the genes associated with these sites are regularly altered in expression. We studied splenic marginal zone lymphomas (MZL) of NFS.V+ mice that are unusual in exhibiting frequent progression from low to high grade, potentially allowing assignment of cancer genes to processes of initiation and progression. We used inverse PCR to clone and analyze 212 retroviral integration sites from 43 MZL at different stages of progression. Sixty-two marked common integration sites and included 31 that had been marked previously. Among the new common integration sites, seven were unique to MZL. Using microarrays and real-time quantitative PIER analysis, we defined differential patterns of gene expression in association with disease progression for Gfi1, Sox4, Brca2, Snf1lk, Nfkb1, Pou2af1, Prdm1, Stat6, and Blnk. Heightened expression of Gfi1 distinguishes MZL from other lymphoma types. The combined use of proviral tagging and analyses of gene expression thus provides a powerful approach to understanding of genes that collaborate in tumorigenesis.

L8 ANSWER 9 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:478879 BIOSIS
DOCUMENT NUMBER: PREV200510270783
TITLE: Expression of ZAP-70 in B cell chronic lymphocytic leukemia is associated with a greater capacity to activate NF kappa B following ligation of surface immunoglobulin.
AUTHOR(S): Castro, Januario E. [Reprint Author]; Prada, Carlos E.; Jose, Jorieth M.; Jung, Scott A.; Chen, Liguang J.; Meraz, Gabriel A.; Kipps, Thomas J.
CORPORATE SOURCE: Univ Calif San Diego, John and Rebecca Moores Canc Ctr, La Jolla, CA 92093 USA
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 769A. Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

AB The NF kappa B transcription factors p50/p65 regulate the expression of genes encoding various growth-promoting factors and anti-apoptotic proteins, such asthe cellular inhibitors of apoptosis (c-IAPs), Caspase-8/Flice-inhibitory protein (FLIP), A I (also known as Bfl1), tumor necrosis factor receptor (TNFR)-associated factor I (TRAF1) and 2 (TRAF2). Furthermore, constitutive activationof NF kappa B has been observed in many tumor types, supporting the notion that activation of NF kappa B can play a causal role in tumor development and/orprogression. Studies have shown chronic lymphocytic leukemia (CLL) cells experience activation of NF kappa B in vitro upon ligation of their surface immunoglobulin (Ig), which commonly possesses polyreactive-binding activity for manyself-antigens. Other studies also have found that CLL cells from different patients vary in their capacity to undergo B-cell-receptor signaling following ligation of their surface Ig receptors, a capacity that appears associated withleukemia-B-cell expression of the zeta-associated protein of 70 kD (ZAP-70). We examined whether CLL B cell expression of ZAP-70 also was associated with the capacity to activate NF kappa B upon surface Ig ligation. For this we used CLL B cells of 8 different patients that expressed ZAP-70 and CLL B cells from8 other patients that had negligible expression of this tyrosine kinase (as assessed by immunoblot and flow cytometric analysis). The CLL B cells of these two groups of patients had similar expression levels of surface, allowing us to use a F(ab')2 anti-human IgM (anti-p) to effect comparable surface Ig receptor ligation. Following treatment with anti-p, we observed early and sustained

degradation of I kappa B-alpha, thereby releasing cytoplasmic p50/p65 to the nucleus - the hallmark of NF kappa B activation. Moreover, this was associated with subsequent increased expression of NFKB target genes. In contrast, similar events were not observed following treatment with anti-p in the cases lacking expression of ZAP-70. Also, activation of NFKB in ZAP-70+ cases was associated with a greater release of intracellular calcium and calcium flux following treatment with anti-p than observed in ZAP-70-negative cases. Both calcium flux and activation of NFKB induced by anti-p in these leukemia cells could be inhibited by Cyclosporine-A, indicating that these responses were mediated via acalmodulin-calcineurin-dependent pathway. These studies reveal that expression of ZAP-70 in B cell CLL is associated with a greater capacity to induce activation of NFKB following ligation of surface Ig, a characteristic that might account for the more aggressive clinical behavior of patients with leukemia B cells that express this tyrosine kinase. Moreover, if constitutive activation via ligation of surface Ig with self-antigen in vivo leads to activation of NFKB, then targeting the calmodulin-calcineurin-dependent pathway might have therapeutic potential for this subset of patients with this disease.

L8 ANSWER 10 OF 22 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 2

ACCESSION NUMBER: 2004450791 EMBASE
TITLE: [Classical Hodgkin's lymphoma: Biology and grey zones]. MALADIE DE HODGKIN CLASSIQUE: BIOLOGIE ET FORMES FRONTIERES.
AUTHOR: Gaulard P.; Brousse N.
CORPORATE SOURCE: P. Gaulard, Departement de Pathologie, Hopital Henri Mondor, 94010 Creteil Cedex, France. philippe.gaulard@hmn.ap-hop-paris.fr
SOURCE: Annales de Pathologie, (2004) Vol. 24, No. 4, pp. 330-348.
Refs: 98
ISSN: 0242-6498 CODEN: ANPADZ
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
025 Hematology
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 4 Nov 2004
Last Updated on STN: 4 Nov 2004

AB Advances in the biology of Hodgkin's lymphoma have lead to the distinction between two entities, "classical" Hodgkin's lymphoma and nodular lymphocyte predominance Hodgkin's lymphoma, previously called nodular paragranuloma, which share distinct clinical aspects. The definition of diagnostic criteria has also been helpful to separate Hodgkin's lymphoma from other lymphomas which can mimick Hodgkin's disease such as anaplastic large cell lymphomas, T-cell/histiocyte rich diffuse large B-cell lymphoma, and some peripheral T-cell lymphomas, mainly angioimmunoblastic-type. Reed-Sternberg cell, the neoplastic cell of "classical" Hodgkin's lymphoma, still retains some secrets. Despite some controversies, there is more and more evidence for a lymphoid B cell origin. The involvement of Epstein-Barr virus, cytokines and/or oncogenes expression in the pathogeny can be suggested, although the precise mechanisms leading to transformation and/or accounting for tumour progression are still elusive. Recently, the roles of the pathway implicating the activation of NFkB as well as the autocrine secretion of interleukin-13 have been demonstrated.

L8 ANSWER 11 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:477023 BIOSIS
DOCUMENT NUMBER: PREV200510268927
TITLE: Cell contact with CLL cells induces defects in T cell differentiation and effector pathways: Impact of silencing specific cytokine production.
AUTHOR(S): Holderried, Tobias A. W. [Reprint Author]; Gorgun, Gullu; Gribben, John G.
CORPORATE SOURCE: Harvard Univ, Sch Med, Dana Farber Canc Inst, Boston, MA 02115 USA
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 273A-274A.
Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

AB Previous studies have suggested that the development and progression of B cellCLL is dependent on interactions between malignant cells and normal components of the immune system. Although the T cell count may be normal or even increased, T cell dysfunction is a feature of CLL, with abnormal CD4/CD8 ratio, impaired mitogen response, and altered expression of surface antigens in response to antigen presentation. We are evaluating the impact of tumor cells on the immune system and have reported differences in gene expression profiles in T cells in previously untreated CLL patients. Specifically, in both CD4 and CD8 T cells we identified defects in genes regulating cytoskeleton formation, intracellular transportation and control of cytokines and chemokines. Analysis of theabnormal gene expression profiles suggested that many such abnormalities are induced by signaling through surface receptors on T cells by interaction with CLL cells or the microenvironment. To detemine the mechanism, we performed ex vivo tumor cell-T cell interaction assays using patient derived serum, transwell membrane and cell contact assays using CLL and CD4 or CD8 T cells from CLL patients and B cells and CD4 or CD8 T cells from healthy donors. Since the majority of the differentially expressed genes were involved in cell cytoskeletonformation and intracellular vesicle transportation pathways, we examined the impact on those specific pathways using proteomics. In keeping with the gene expression profiles in the T cells of CLL patients, we noted significant decreased expression of NFkB p65 and GDI1 and increase in Arp2/3 in healthy CD4 T cells and decreased expression of Rho-GAP and increased Arp2/3 in healthy CD8 T cells following CLL-T cell contact compared to healthy B cell-T cell contact. In contrast there was no change after exposure to patient sera or tumor cell derived soluble factors for 48h. To further analyze whether tumor cell derived cytokines have an impact oil T cells in CLL, we inhibited IL-10 and IL-4 production in CLL cells and healthy B cells using siRNA targeting IL-10 and/or IL-4. The transfection efficiency monitored by flow cytometry with fluorescence labeled non-silencing RNA and observed 60-98 % transfection efficiency and at 48h observed 40-85% inhibition in IL-10 protein expression. After 48 It incubation of autologous and allogeneic CD4 or CD8 T cells from CLL and healthy donors with non-transfected, mock transfected or IL-10 siRNA transfected CLL or healthy B cells for 48h, T cells were isolated and there was no significant difference in expression of cytoskeletal proteins in both CD4 or CD8 T cells. Addition of anti-IL-10 neutralizing monoclonal antibody also had no effect. Although no effect was noted on cytoskeletal proteins, after incubation with CLL but not healthy B cells, silencing or neutralization of IL-10 induced changes in expression of CXCR1, CXCR2, CXCR3, CXCR4 and CCR5 in CD4 and CCR5 and CCR4 in CD8 cells front healthy donors. We conclude that cell contact with CLL cells induces changes in expression of cytoskeletal proteins in healthy T cells

similar to those observed in T cells from CLL patients and this is not induced by soluble factors including IL-10. However, IL-10 and potentially other soluble factors induce changes in chemokines and chemokine receptors on T cells, suggesting multiple mechanisms impair T cell function in CLL cells. Ongoing studies are assessing ways to repair the defects identified here to enhance immune responsiveness in this disease.

L8 ANSWER 12 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:476312 BIOSIS
DOCUMENT NUMBER: PREV200510268216
TITLE: NF kappa B activation in primary mediastinal large B-cell lymphoma: Nuclear localization of c-REL and coordinate Upregulation of NF kappa B target genes.
AUTHOR(S): Feuerhake, Friedrich [Reprint Author]; Kutok, Jeffery L.; Monti, Stefano; Cattoretti, Giorgio; Kurtin, Paul; Pinkus, Geraldine S.; de Leval, Laurence; Harris, Nancy L.; Savage, Kerry J.; Habermann, Thomas M.; Dalla-Favera, Riccardo; Golub, Todd R.; Aster, Jon C.; Shipp, Margaret A.
CORPORATE SOURCE: Dana Farber Canc Inst, Boston, MA 02115 USA
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 73A. Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

AB Primary mediastinal large B-cell lymphoma (MLBCL) is a clinically distinct entity that typically presents as localized, sclerotic disease in young, female patients. We previously characterized the transcriptional profiles of MLBCLs and identified important shared features with a clinically related disorder, classical Hodgkin lymphoma (cHL) (Blood 102:3871, 2003). Given the documented role of the NFkB survival pathway in Hodgkin Reed-Stemberg cells, we previously assessed NFkB activation in MLBCL by determining the subcellular location of the c-REL subunit of the NFkB heterodimer with a 2-color immunofluoresence assay. In a small pilot MLBCL series, c-REL was localized to the nucleus in the majority of examined cases, consistent with NFkB activation. In the current study, we evaluated c-REL subcellular localization in an additional series of MLBCLs and DLBCLs using a broadly applicable immunoperoxidase method. 100% of MLBCLs exhibited nuclear c-REL staining whereas DLBCL c-REL subcellular localization was more variable. Thereafter, we analyzed the transcription profiles of the34 MLBCLs and 176 DLBCLs for coordinate expression of NFkB target genes, using literature-curated NFkB target gene lists from three independent sources andgene set enrichment analysis (GSEA). MLBCL signatures exhibited significant enrichment of 2 of the 3 NFkB target gene sets. In addition, 32 NFkB target genes from the combined set were significantly more abundant in MLBCLs than DLBCLs (> 30% more abundant and > 99(th) percentile in permutation analysis). Similar results were obtained in an independent series of MLBCLs and DLBCLs with available gene expression profiles (J. Exp. Med. 198:851, 2003). To assess the role of c-REL amplification in NFkB activation in our lymphoma series,we compared c-REL amplification, c-REL subcellular localization and coordinate expression of the identified NFkB target genes and classified the DLBCLs according to putative cell of origin. The majority of c-REL amplifications (67%) were found in DLBCLs of germinal center (GC) subtype, consistent with the observation that c-REL is part of the

described GC signature. However, most (71 %)of the examined GC DLBCLs had cytoplasmic c-REL expression and the GC DLBCLs did not have increased expression of NFkB target genes. Taken together with the MLBCL analyses, these studies indicate that: 1) NFkB is consistently activated in MLBCL; 2) c-REL amplification is not closely associated with NFkB activation in large cell lymphomas (LCLs); and 3) NFkB activation in LCL subtypes does not require amplification of the c-REL locus.

L8 ANSWER 13 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:476098 BIOSIS
DOCUMENT NUMBER: PREV200510268002
TITLE: Activation of classical and alternative nuclear factor-kappaB (NF-kB) pathways in diffuse large B -cell lymphomas.
AUTHOR(S): Timar, Botond [Reprint Author]; Chadburn, Amy; Knowles, Daniel; Cesarman, Ethel
CORPORATE SOURCE: Cornell Univ, Weill Med Coll, New York, NY USA
SOURCE: Blood, (NOV 16 2004) Vol. 104, No. 11, Part 1, pp. 12A-13A. Meeting Info.: 46th Annual Meeting of the American-Society-of-Hematology. San Diego, CA, USA. December 04 -07, 2004. Amer Soc Hematol. CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

AB Activation of the NF-kB pathway is involved in many human neoplasms. In this study we examined the status of the NF-kB canonical (IkB, p50/p65) and non-canonical (p52, RelB) pathways in diffuse large B-cell lymphomas (DLBCL), which are a common and heterogeneous group of lymphoid malignancies. DLBCL have been divided into activated B-cell (ABC) like, and germinal center B-cell (GCB) likesubgroups, which have been reported to have high and low NF-kB activity, respectively. However, the nature of the NF-kB complexes in this lymphoma entity has not been previously evaluated. Therefore we performed Western blotting, electrophoretic mobility shift assays (EMSA) and real time quantitative RT-PCRs on nuclear and cytoplasmic protein and total RNA extracts in 20 primary tumor samples and 9 different DLBCL cell lines. In the cell lines, presence of NFkB proteins in nuclear extracts correlated with expression of NF-kB target genes (CCR7, IkBa, CCND2, BCL-2, IRF4) as determined by RT-PCR. Therefore, these could be assigned into GCB and ABC-like categories. In primary DLBCLs, EMSA showedNFAB binding in all but one case. The same cases (19/20) had high p52 in the nucleus indicating activation of the alternative pathway. TNF family ligand BAFF was also found to be expressed in all primary samples and most cell lines. The classical pathway, as determined by nuclear p50, was also present in thesecases. Levels of p65 and ROB expression were variable, but did not correlate with the mRNA expression of NF-kB target genes. In conclusion, while DLBCL cell lines may be divided into two distinct categories, the primary samples represented a spectrum of NF-kB target gene activity, while levels of NF-kB expression were high. BAFF expression and activation of the alternative pathway may be important in the pathogenesis of DLBCL.

L8 ANSWER 14 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:155378 BIOSIS
DOCUMENT NUMBER: PREV200400148683
TITLE: PS341 inhibits cell proliferation, induces apoptosis of and enhances the biological effects of rituximab on non-Hodgkin's lymphoma (NHL) cell lines and lymphoma

xenografts.
AUTHOR(S): Hernandez-Ilizaliturri, Francisco J. [Reprint Author]; Kotowski, Adam; Czuczman, Myron S. [Reprint Author]
CORPORATE SOURCE: Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 903a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB The ubiquitin-proteasome system plays a significant role in tumor growth and progression. Deregulation of the NFkB/IkBa pathway by ubiquitinization and proteasome degradation of IkBa has been observed in several NHL subtypes. Increased NFkB activity leads to an aberrant regulation of cell cycle/anti-apoptotic proteins, PS341, a proteasome inhibitor induces arrest in cell cycle progression of and apoptosis in various pre-clinical models. Proteasome inhibition enhances the cytotoxic effects of chemotherapy. Effects of PS341 on rituximab antitumor activity need to be defined. Objective: To evaluate the effects of PS341 in combination with rituximab against B-cell lymphoma. Material and Methods: In vitro: A lymphoma cell line panel representing various subtypes of NHL were exposed to different concentrations of PS341 (2 and 20nM) in the presence of rituximab, istoype or RPMI. Standard (3H)-Thymidine incorporation assays were performed to assess DNA synthesis at 24 and 48 hrs. In addition, lymphoma cells were treated with PS341 +/- rituximab to evaluate induction of apoptosis as determined by flow cytometry. For ADCC/CMC studies, 51Cr-labeled NHL cells were exposed to PS341 prior to treatment with rituximab (10mg/ml) and peripheral blood mononuclear cells (Effector: Target ratio 40:1) or human serum, respectively. 51Cr-release was measured and the percentage of lysis was calculated. Statistical analysis of results was performed using the Chi-square test. For in vivo studies, 6-8-week old SCID mice were inoculated via tail vein injection with (1X106) Raji cells. Animals were then assigned to receive placebo, PS341 (1mg/kg/dose), rituximab (10mg/kg/dose) or PS341 preceding each dose of rituximab. PS341 and rituximab were administered via tail vein injection for a total of 4 doses each. Following therapy, mice were observed for survival defined as time to appearance of limb paralysis. Results: Exposure of various lymphoma cell lines to PS341 resulted in a significant decrease in cell proliferation. In addition, PS341 in combination with rituximab induced a higher degree of apoptosis and CMC on Raji, DHL-4 and SKW cell lines. Treatment of lymphoma-bearing SCID mice with PS341 given prior to each rituximab dose resulted in better disease control and longer survival than treatment with either agent alone (p=0.018). Up to date, 60% of animals treated with rituximab and PS341 remain alive and disease-free as compared to 20% in the rituximab alone treated group. Conclusion: Proteasome inhibition by PS341 induces apoptosis, cell growth arrest and renders various NHL cell lines more susceptible to rituximab-associated CMC. In vivo, administration of PS341 with rituximab was more effective in controlling lymphoma growth and in prolonging survival than rituximab or PS341 monotherapy alone.

L8 ANSWER 15 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:155282 BIOSIS
DOCUMENT NUMBER: PREV200400148642
TITLE: MALT1 expression in normal and neoplastic lymphoid tissues: Strong expression characterizes t(14;18)(q32;q21) of MALT

lymphoma.

AUTHOR(S): Ye, Hongtao [Reprint Author]; Liu, Hongxiang [Reprint Author]; Shirali, Sima [Reprint Author]; Chott, Andreas; Streubel, Berthold; Siebert, Reiner; Gesk, Stefan; Radford, John A.; Banerjee, Sankar; Isaacson, Peter G.; Dogan, Ahmet; Du, Ming-Qing [Reprint Author]

CORPORATE SOURCE: Division of Molecular Histopathology, Department of Pathology, University of Cambridge, Cambridge, UK

SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 892a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004

AB The MALT1 gene is involved in t(11;18)(q21;q21) and t(14;18)(q32;q21) of MALT lymphoma. In t(11;18), the C-terminal of the MALT1 gene is fused with the N-terminal of the API2 gene, forming an API2-MALT1 fusion, while in t(14;18), the MALT1 gene is juxtaposed to the IGH locus, deregulating its expression. MALT1 interacts with BCL10, which is involved in t(1;14)(p22;q32) of MALT lymphoma, and synergistically activates NFkB. BCL10 specifically links the antigen receptor signaling to NFkB pathway in both B and T-cells. In view of the biological interaction between MALT1 and BCL10, MALT1 may play a role similar to BCL10 in normal B-cells and their malignancies. We examined MALT1 expression in various normal tissues and B-cell lymphomas by immunohistochemistry using mouse monoclonal antibodies to both N- and C-terminal MALT1. MALT1 protein was expressed in lymphoid tissues but not in 20 other types of normal tissues. In normal B-cell follicles, MALT1 expression pattern was identical to that of BCL10; high in the cytoplasm of the germinal center B cells, but weak or absent in the mantle and marginal zone B cells. In MALT lymphoma, MALT1 expression varied, ranging from negative to strong cytoplasmic expression. In three MALT lymphomas with cytogenetically proven t(14;18)(q32;q21), strong cytoplasmic MALT1 expression was seen in each case. Interestingly, these cases also showed an increased cytoplasmic BCL10 expression. Similar MALT1 and BCL10 expression patterns were observed in 3 of 41 (7%) MALT lymphomas from the orbit but not in those from the stomach (125), lung (26), salivary gland (57), skin (18), thyroid (12), conjunctiva (8) and liver (5). Two of the three orbital MALT lymphomas with MALT1 and BCL10 expression pattern similar to those with t(14;18) were further investigated by interphase FISH and were shown to harbor IGH and MALT1 breakpoints suggesting/indicating presence of t(14;18) in both cases. In follicular and mantle cell lymphoma, MALT1 expression was similar to their normal cell counterparts. In diffuse large B-cell lymphoma, MALT1 expression varied, with majority expressing at moderate levels. These results show that MALT1 expression pattern is identical to that of BCL10 in normal lymphoid tissues and varies in MALT lymphomas, with high cytoplasmic expression of both MALT1 and BCL10 in those with t(14;18).

L8 ANSWER 16 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:173655 BIOSIS

DOCUMENT NUMBER: PREV200400172646

TITLE: The molecular signature of mediastinal large B-cell lymphoma differs from that of other diffuse large B-cell lymphomas and shares features with classical Hodgkin's lymphoma.

AUTHOR(S): Savage, Kerry J. [Reprint Author]; Monti, Stefano; Kutok, Jeff; Cattoretti, Giorgio; Neuberg, Donna; Laval, Laurence; Kurtin, Paul; Del Chin, Paola; Ladd, Christine; Feuerhake, Friedrich [Reprint Author]; Aguiar, Ricardo [Reprint Author]; Li, Sigui; Salles, Gilles; Berger, Francoise; Jing, Wen; Pinkus, Geraldine S.; Habermann, Thomas; Dalla-Favera, Riccardo; Harris, Nancy Lee; Aster, Jon C.; Golub, Todd R.; Shipp, Margaret A. [Reprint Author]

CORPORATE SOURCE: Medical Oncology, Dana-Farber Cancer Institute, Boston, MA, USA

SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 179a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 31 Mar 2004
Last Updated on STN: 31 Mar 2004

AB Mediastinal large B-cell lymphoma (MLBCL) is a recently identified subtype of diffuse large B-cell lymphoma (DLBCL) that typically presents as localized tumors in young female patients. Although the diagnosis of MLBCL is based on clinical and pathologic features, MLBCL patients also clinically resemble those with the nodular sclerosis subtype of classical Hodgkin's lymphoma (cHL). To elucidate the molecular features of MLBCL, we compared the gene expression profiles of newly diagnosed MLBCLs (n=34) and DLBCLs (n=176) and developed a classifier of these diseases. The top 15,000 genes from the U133A and U133B Affymetrix oligonucleotide microarrays were selected based on their ranking by median absolute deviation across all samples. The genes were then sorted by their degree of correlation with the MLBCL vs. DLBCL class distinction according to the signal-to-noise metric. Permutation of the sample labels indicated that MLBCL had significantly lower expression of over 1000 genes and significantly higher expression of over 1000 additional genes, in comparison to DLBCLs ($p<.01$). The MLBCL transcriptional signature included MAL and FIG1 - genes previously reported to be highly expressed in this disease. MLBCLs had significantly lower expression of multiple components of the B-cell receptor signaling cascade, including IgM, BLK, BLNK and PKCb, a profile resembling that of cHL Reed-Sternberg cells. Like cHL, MLBCLs also had increased expression of the IL13 receptor and downstream effectors of IL13 signaling, JAK2 and STAT1, in addition to multiple TNF family members and TRAF1. The observed similarities between cHL and MLBCL were confirmed with a formal enrichment test. Increased expression of STAT1 and TRAF1 protein in MLBCL tumor cells was also documented by immunohistochemistry. Given the increased TRAF1 expression and known link to NFkB, MLBCLs were also evaluated for nuclear translocation of c-REL protein. In almost all cases, c-REL was localized to the nucleus, consistent with activation of the NFkB pathway. These studies identify a molecular link between MLBCL and cHL and a shared survival pathway. In addition, the analysis defines molecular differences in morphologically similar tumors (MLBCL vs. DLBCL) and identifies shared features of morphologically distinct neoplasms (MLBCL and cHL).

L8 ANSWER 17 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:173515 BIOSIS

DOCUMENT NUMBER: PREV200400172549

TITLE: Pathways involved in the emergence of resistance to rituximab in non-Hodgkin's lymphoma (NHL) cell lines.

AUTHOR(S): Czuczman, Myron S. [Reprint Author]; Testa, James Jr. [Reprint Author]; Brombos, Dana [Reprint Author];

Hernandez-Ilizaliturri, Francisco J. [Reprint Author]
CORPORATE SOURCE: Medicine, Roswell Park Cancer Institute, Buffalo, NY, USA
SOURCE: Blood, (November 16 2003) Vol. 102, No. 11, pp. 103a. print.
Meeting Info.: 45th Annual Meeting of the American Society of Hematology. San Diego, CA, USA. December 06-09, 2003. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Mar 2004
Last Updated on STN: 31 Mar 2004

AB Rituximab has changed the treatment paradigm for B-cell lymphoma patients. Strategies combining rituximab with various chemotherapy regimens have resulted in higher antitumor activity and improved survival in several subtypes of lymphoma as compared to chemotherapy alone. However, despite its antitumor activity, not every patient responds to rituximab and a significant number of patients relapse after an initial response. Failures following rituximab are presumed largely the consequence of acquired resistance. In an attempt to define the molecular basis responsible for the development of resistance to rituximab we have developed several rituximab-resistant cell lines (2R and 4RH) derived from rituximab-sensitive lymphoma cells (Raji parental). Objective: To study global gene profile changes occurring upon development of resistance to rituximab and to validate genetic changes at the post-transcriptional level. Material and Methods: Studies were conducted in Raji parental cells and Raji rituximab-resistant cells (2R and 4RH). Resistant clones were generated by chronic exposure of Raji cells to escalating doses of rituximab with (4RH) or without (2R) human complement. Functional assays were performed to demonstrated decrease in rituximab sensitivity on 2R and 4RH cells. Subsequently, total RNA was extracted from each cell line (Raji, 2R or 4RH) and cDNA were generated. Labeled cDNA was hybridized using the Roswell Park Cancer Institute Cancer Chip, containing 11,519 cDNAs, and then scanned to obtain quantitative gene expression levels. Data was analyzed by Genomic Core Facilities, Department of Genetics, RPCI. Post-transcriptional validation of specific gene changes was performed by protein electrophoresis and immunoblotting. Results: Acquirement of resistance to rituximab was associated with several gene expression changes. Similar gene expression changes were observed between 2R and 4RH cells. Upregulation of 129 genes and downregulation of 10 genes were observed in both of the rituximab-resistant cell lines as compared to Raji cells. Particularly, genes regulating the ubiquitin-proteasome system, NFk-B/IkB pathway, and anti-apoptotic genes were overexpressed on 2R and 4RH cells. Post-transcriptional studies demonstrated that the expression of the ubiquitin-activating (E1) and ubiquitin-conjugating (E2) enzymes, NFkB transcription factor, and anti-apoptotic proteins, survivin and Bcl-2, was increased on rituximab-resistant cells. Concomitantly, downregulation of IkB was observed in rituximab-resistant cells as compared to parental cells. Conclusions: Post-transcriptional validation of cDNA microarray studies demonstrated that rituximab resistance is associated with protein changes in key regulators of the ubiquitin-proteasome system (E1 and E2), apoptosis (Bcl-2 and survivin) and nuclear transcriptional factors (NFkB and IkB). Our data strongly suggests that the acquirement of resistance to rituximab is associated with deregulation in the ubiquitin-proteasome system leading to an increase in NFkB activity. In addition, protein degradation of IkB, enhanced by upregulation of E1/E2, contributes to further upregulation of NFkB activity. These changes result in an increased transcription of genes that inhibit apoptosis (Bcl-2 and survivin) and render lymphoma cells resistant to rituximab.

L8 ANSWER 18 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on

STN

ACCESSION NUMBER: 2003:335954 BIOSIS
DOCUMENT NUMBER: PREV200300335954
TITLE: Constitutively Active AKT (Protein Kinase B) and Differential Regulation of Its Isoforms in Malignant Lymphomas.
AUTHOR(S): Fillmore, Chris G. [Reprint Author]; Wang, Qifu [Reprint Author]; Carey, Michael J. [Reprint Author]; Elenitoba-Johnson, Kojo S. J. [Reprint Author]; Lim, Megan S. [Reprint Author]
CORPORATE SOURCE: Department of Pathology, University of Utah, Salt Lake City, UT, USA
SOURCE: Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 1354. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003

AB AKT (Protein Kinase B) is involved in the regulation of many mediators of cell survival and apoptotic stimuli including DNA damage, cytokines, and chemotherapeutic agents. Phosphorylated (active) AKT exerts its anti-apoptotic effect through phosphorylation of BAD, caspase 9, NFkB, and the forkhead transcription factor. Three isoforms of AKT have been identified: AKT-1, -2 and -3, and expression of each may be tissue-specific. Furthermore, selective regulation of specific AKT isoforms by EGF and TCL1 has been described. AKT is expressed in T- and B-lymphocytes, and activated in response to cytokine and antigen-receptor stimulation. It is also a critical component of the IL-2 family cytokine survival signal. To date, the role of AKT signaling and the levels of expression of its isoforms in malignant lymphomas have not been reported. To determine whether AKT signaling is enhanced in human malignant lymphomas and to identify the expression patterns of AKT isoforms in these neoplasms, we studied the expression of AKT-1, -2, and -3, in 36 cell lines derived from hematopoietic neoplasms by RT-PCR and western blot analysis. The in-situ level of phosphorylated AKT was studied in 72 human malignant B-cell non-Hodgkin's lymphoma tissues (12 small lymphocytic, 19 follicular, 6 marginal zone, 15 mantle cell, and 20 diffuse large B-cell lymphomas). The effect of IL-2 stimulation on the expression of AKT isoforms and active AKT was studied in cell lines (Jurkat, SUDHL-1, Karpas 299) derived from human T-cell malignancies. Western blot and RT-PCR analyses revealed that the majority of hematopoietic cell lines (95%) expressed all three of the AKT isoforms. The levels of AKT-1 expression were uniform, but AKT-2 and AKT-3 were expressed at variable levels. In addition, there was constitutive expression of active phosphorylated AKT in 23/36 (64%) of the cell lines and 33/72 (46%) of the NHL tissues. Immunohistochemical studies demonstrated nuclear localization of phosphorylated AKT in 40% of NHL tissues. Investigation of functional regulation of AKT isoforms by IL-2 showed that while AKT-1 mRNA levels were unaffected, the levels of AKT-2 mRNA were up-regulated and AKT-3 mRNA levels were down regulated in Jurkat, SUDHL-1 and Karpas 299 cells. IL-2 stimulation resulted in upregulation of phosphorylated AKT in the SUDHL-1 and Jurkat, but not Karpas 299, cell lines. The constitutive activation of AKT seen in human lymphoma tissues and cell lines supports its proposed key role in lymphoma cell survival. Furthermore, there is differential regulation of AKT isoform expression by IL-2, suggesting an importance in the survival pathway mediated by IL-2. Future studies to determine the substrates of AKT-2 and -3 will be important in elucidating the pathobiology of

lymphomagenesis.

L8 ANSWER 19 OF 22 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:186532 BIOSIS
DOCUMENT NUMBER: PREV200200186532
TITLE: Expression of IL-12 and IL-18 receptors in human neoplastic B cells.
AUTHOR(S): Pistoia, Vito [Reprint author]; Guglielmino, Roberta [Reprint author]; Corcione, Anna [Reprint author]; Truini, Mauro [Reprint author]; Airoldi, Irma [Reprint author]
CORPORATE SOURCE: Oncology Lab, G. Gaslini Institute, Genova, Italy
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 330a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Mar 2002
Last Updated on STN: 13 Mar 2002

AB Interleukin 12 is an immunomodulatory cytokine that activates murine and human B cells after binding to its specific receptor. The three main B cell subsets purified from human tonsils, i.e. naive (IgD+), germinal center (IgD-, CD38+) and memory (IgD-, CD38-) B cells, constitutively express the two chains (beta 1 and beta 2) of the IL-12 receptor (IL-12R). However, the IL-12R is functional only in naive B cells, to which it signals through the NFkB pathway (Airoldi I. et al., J. Immunol. 165:6880-6888, 2000). The IL-18 receptor (IL-18R) is composed of two chains, i.e. accessory protein-like (AcPL) and IL-1 receptor related protein (IL-1Rrp), and is expressed in tonsil B lymphocytes exclusively after stimulation with IL-12. Furthermore, IL-12 and IL-18 synergize in the induction of interferon-gamma production by activated tonsil B lymphocytes (Airoldi I. et al., J. Immunol. 165:6880-6888, 2000). Here we have investigated the expression of IL-12 and IL-18 receptor genes in three types of human B-cell lymphoma originating from normal naive, germinal center and memory B cells and designated as Mantle Cell Lymphoma (MCL), Follicular Lymphoma (FL) and Marginal Zone Lymphoma (MZL), respectively. The same studies have been performed with a panel of Burkitt's lymphoma (BL) cell lines, either EBV-positive or EBV-negative. RNA was extracted from neoplastic B cells freshly isolated from the lymph nodes of 3 MCL, 4 FL and 2 MZL patients, as well as from 8 BL cell lines. RNA was subsequently reverse transcribed and subjected to PCR using pairs of primers specific for the two chains of the IL-12R and of the IL-18R, respectively. All neoplastic B lymphocytes expressed the IL-12R beta 1, but not the beta 2, chain irrespective of their origin. The two chains of the IL-18R showed heterogenous patterns of expression: AcPL alone was detected in 1/4 FL, 0/3 MCL, 0/2 MZL, 0/8 BL cell lines; IL-1Rrp alone was expressed in 1/4 FL, 0/3 MCL, 0/2 MZL, 0/8 BL cell lines. The complete IL-18R was detected in 5 cases of B -cell lymphoma (2/4 FL, 2/3 MCL, 1/2 MZL). The consistent absence of the IL-12R beta 2 chain, together with the presence of one or both chains of the IL-18R, in neoplastic B cells freshly isolated from different tumors represent important phenotypic differences among such tumors and their presumed normal counterparts. Our working hypothesis is that these changes are related to malignant B cell trasformation. Experiments are now in progress to i) investigate the function of the IL-18R in B lymphoma cells and ii) reconstitute the complete IL-12R in malignant B cells by trasfecting IL-12R beta 2 chain negative BL cell lines with a beta 2 chain bearing expression vector (kindly provided by L. Rogge and F. Sinigaglia, Roche Milano Ricerche,

Italy) for future functional studies.

L8 ANSWER 20 OF 22 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:955798 SCISEARCH
THE GENUINE ARTICLE: 497JF
TITLE: CD40 employs p38 MAP kinase in IgE isotype switching
AUTHOR: Brady K; Fitzgerald S; Ingvarsson S; Borrebaeck C A K; Moynagh P N (Reprint)
CORPORATE SOURCE: Univ Coll Dublin, Conway Inst Biomol & Biomed Res, Dept Pharmacol, Foster Ave, Blackrock, Co Dublin, Ireland (Reprint); Univ Coll Dublin, Conway Inst Biomol & Biomed Res, Dept Pharmacol, Blackrock, Co Dublin, Ireland; Lund Univ, Dept Immunotechnol, Lund, Sweden
COUNTRY OF AUTHOR: Ireland; Sweden
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (23 NOV 2001) Vol. 289, No. 1, pp. 276-281.
ISSN: 0006-291X.
PUBLISHER: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 27
ENTRY DATE: Entered STN: 14 Dec 2001
Last Updated on STN: 14 Dec 2001

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB IgE switching requires the prior induction of CE germline transcripts which is mediated by the concerted binding of STAT-6 and NF kappaB to the CE promoter. These transcription factors are regulated by IL-4 and CD40, respectively. However the latter can effect other signaling pathways and the present study explores the role of p38 MAPK in induction of CE germline transcripts. CD40 and IL-4, both alone and in synergy, were initially shown to activate the CE promoter in a B cell lymphoma cell line. Under the same conditions CD40 caused activation of p38 MAPK, whereas IL-4 was ineffective. The p38 MAPK inhibitor, SB203580, and a dominant negative form of p38 MAPK decreased the CD40 activation of the CE promoter by reducing the ability of CD40 to increase the transactivation potential of NF kappaB. This study suggests that p38 MAPK is crucially important in mediating CD40 activation of NFKB which acts to induce CE germline transcripts, ultimately facilitating IgE switching. (C) 2001 Academic Press.

L8 ANSWER 21 OF 22 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:820641 HCAPLUS
DOCUMENT NUMBER: 134:83972
TITLE: Bcl-2 intersects the NFκB signalling pathway and suppresses apoptosis in ventricular myocytes
AUTHOR(S): Kirshenbaum, Lorrie A.
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine, University of Manitoba, Winnipeg, MB, Can.
SOURCE: Clinical and Investigative Medicine (2000), 23(5), 322-330
CODEN: CNVMDL; ISSN: 0147-958X
PUBLISHER: Canadian Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As a first step toward identifying putative regulators of apoptosis in the heart, the impact of the anti-apoptosis protein Bcl-2 (B-cell lymphoma gene) on the NFκB (nuclear factor kappa beta) signalling pathway in suppressing apoptosis in ventricular myocytes was studied. The data indicate that adenovirus-mediated delivery of Bcl-2 resulted in a significant increase in NFκB-dependent DNA binding and NFκB-directed gene transcription. No change in NFκB protein content was observed in myocytes expressing Bcl-2.

Moreover, the Bcl-2-mediated NFκB activation was found to be related to changes in the activity of the NFκB regulatory protein IκBα (inhibitor of kappa beta). In this regard, a marked reduction in IκBα protein content was observed in ventricular myocytes expressing Bcl-2. The mode by which Bcl-2 regulates IκBα was related to the N-terminal phosphorylation and degradation of IκBα by the proteasome since an N-terminal deletion mutant of IκBα or the proteasome inhibitor lactacystin abrogated Bcl-2's inhibitory effects on IκBα and prevented NFκB activation. Furthermore, adenovirus-mediated delivery of a phosphorylation defective form of IκBα rendered ventricular myocytes incapable of NFκB activation and susceptible to tumor necrosis factor alpha-mediated apoptosis. Moreover, Bcl-2's anti-apoptotic function was lost in cells defective for NFκB activation. The data provide evidence for a link between Bcl-2 and the NFκB signalling pathway for the suppression of apoptosis in ventricular myocytes.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 22 MEDLINE on STN
ACCESSION NUMBER: 92103674 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1760839
TITLE: B cell lymphoma-associated chromosomal translocation involves candidate oncogene lyt-10, homologous to NF-kappa B p50.
AUTHOR: Neri A; Chang C C; Lombardi L; Salina M; Corradini P; Maiolo A T; Chaganti R S; Dalla-Favera R
CORPORATE SOURCE: Department of Pathology, College of Physicians and Surgeons, Columbia University, New York, New York 10032.
CONTRACT NUMBER: CA-20194 (NCI)
CA-34775 (NCI)
CA-44029 (NCI)
SOURCE: Cell, (1991 Dec 20) Vol. 67, No. 6, pp. 1075-87.
Journal code: 0413066. ISSN: 0092-8674.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199202
ENTRY DATE: Entered STN: 2 Mar 1992
Last Updated on STN: 3 Feb 1997
Entered Medline: 11 Feb 1992

AB A B cell lymphoma-associated chromosomal translocation, t(10;14)(q24;q32), juxtaposes the immunoglobulin C alpha 1 locus to a novel gene, lyt-10. The normal lyt-10 cDNA codes for a 98 kd protein which displays amino-terminal homology with the rel (DNA-binding) domain of the NF-kappa B-rel family of transcription factors and carboxy-terminal homology with the NF-kappa B p50 precursor protein, including the putative proteolytic cleavage domain (poly-G) and the ankyrin-like repeat domains. The lyt-10 protein can bind to kappa B sequences in vitro, although with different specificity from NF-kappa B p50, and in vitro DNA-binding is activated by removal of the ankyrin domain. Chromosomal translocation generates an lyt-10-C alpha 1 fusion gene coding for a protein that retains the rel effector domain, lacks the ankyrin regulatory domain, and binds kappa B sequences in vitro, suggesting its constitutive activation in vivo. Analogous rearrangements of the lyt-10 gene have been found in an additional three cases of lymphoid neoplasia. The lyt-10 gene defines a new subfamily (rel/poly-G/ankyrin) of NF-kappa B-rel transcription factors with potential for oncogenic activation in human cancer.

=> d his

```
     (FILE 'HOME' ENTERED AT 15:00:23 ON 29 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 15:00:55 ON 29 JAN 2007
L1          3538 S BCL-6
L2          3466 S "NFKB"
L3             0 S L1 AND L2
L4           265 S LAZ3 OR "ZINC FINGER PROTEIN 51"
L5             0 S L2 AND L4
L6         49561 S "B CELL CLL" OR "B CELL LYMPHOMA"
L7            24 S L6 AND L2
L8            22 DUP REM L7 (2 DUPLICATES REMOVED)

=> e nadler s g/au
E1            10      NADLER S D/AU
E2           146      NADLER S F/AU
E3           177 --> NADLER S G/AU
E4             1      NADLER S G */AU
E5            30      NADLER S H/AU
E6            61      NADLER S P/AU
E7             2      NADLER S S/AU
E8            25      NADLER S T/AU
E9             4      NADLER SAM/AU
E10            5      NADLER SAMUEL/AU
E11            8      NADLER SAMUEL B/AU
E12           21      NADLER SAMUEL T/AU

=> s e3
L9          177 "NADLER S G"/AU

=> e neubauer m g/au
E1             4      NEUBAUER M E/AU
E2             6      NEUBAUER M F/AU
E3            74 --> NEUBAUER M G/AU
E4             3      NEUBAUER M J/AU
E5             6      NEUBAUER M L/AU
E6             1      NEUBAUER M P/AU
E7           317      NEUBAUER M S/AU
E8             9      NEUBAUER MANFRED/AU
E9             3      NEUBAUER MARC S/AU
E10            8      NEUBAUER MARCUS/AU
E11           13      NEUBAUER MARCUS A/AU
E12            1      NEUBAUER MAREIKE/AU

=> s e3
L10           74 "NEUBAUER M G"/AU

=> e feder j n/au
E1           119      FEDER J L/AU
E2            74      FEDER J M/AU
E3           190 --> FEDER J N/AU
E4             1      FEDER J N */AU
E5            16      FEDER JACK B/AU
E6             1      FEDER JAN DAVID/AU
E7             1      FEDER JEAN M/AU
E8             3      FEDER JEAN MARC/AU
E9             1      FEDER JEFFREY/AU
E10           75      FEDER JEFFREY L/AU
E11           92      FEDER JENS/AU
E12            1      FEDER JOHANN/AU

=> s e3
L11         190 "FEDER J N"/AU
```

```
=> e carman j/au
E1            2     CARMAN III F S/AU
E2            4     CARMAN IRENA/AU
E3          105 --> CARMAN J/AU
E4           83     CARMAN J A/AU
E5            1     CARMAN J ANTHONY/AU
E6           75     CARMAN J B/AU
E7           12     CARMAN J C/AU
E8            1     CARMAN J D/AU
E9            6     CARMAN J E/AU
E10           1     CARMAN J F/AU
E11         128     CARMAN J G/AU
E12          13     CARMAN J H/AU

=> s e3
L12         105 "CARMAN J"/AU

=> d his

     (FILE 'HOME' ENTERED AT 15:00:23 ON 29 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 15:00:55 ON 29 JAN 2007
L1          3538 S BCL-6
L2          3466 S "NFKB"
L3             0 S L1 AND L2
L4           265 S LAZ3 OR "ZINC FINGER PROTEIN 51"
L5             0 S L2 AND L4
L6         49561 S "B CELL CLL" OR "B CELL LYMPHOMA"
L7            24 S L6 AND L2
L8            22 DUP REM L7 (2 DUPLICATES REMOVED)
                 E NADLER S G/AU
L9           177 S E3
                 E NEUBAUER M G/AU
L10           74 S E3
                 E FEDER J N/AU
L11          190 S E3
                 E CARMAN J/AU
L12          105 S E3

=> s l9 or l10 or l11 or l12
L13         538 L9 OR L10 OR L11 OR L12

=> s l13 and l8
L14           0 L13 AND L8

=> s l13 and l2
L15           4 L13 AND L2

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16           4 DUP REM L15 (0 DUPLICATES REMOVED)

=> d 1-4 ibib ab

L16   ANSWER 1 OF 4  BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-23119  BIOTECHDS
TITLE:            New nucleic acid or the cDNA sequence included in ATCC
                  Deposit No:PTA-2671 encoding imidazoline receptor related
                  protein 1 or imidazoline receptor related protein 1b, useful
                  in diagnosing, treating or preventing e.g., kidney tumors;
                     for kidney cancer and neurodegenerative disorder
                     diagnosis, prevention and therapy
```

AUTHOR: FEDER J N; KINNEY G G; MINTIER G; RAMANATHAN C S; BOL D K; RYSECK R
PATENT ASSIGNEE: BRISTOL-MYERS SQUIBB CO
PATENT INFO: WO 2004084810 7 Oct 2004
APPLICATION INFO: WO 2004-US8207 16 Mar 2004
PRIORITY INFO: US 2003-395812 21 Mar 2003; US 2003-395812 21 Mar 2003
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-710258 [69]

AB DERWENT ABSTRACT:

NOVELTY - A new isolated nucleic acid molecule or the cDNA sequence included in ATCC Deposit No:PTA-2671 comprises a sequence encoding an imidazoline receptor related protein 1 or imidazoline receptor related protein 1ba, or its fragment, domain or epitope.

DETAILED DESCRIPTION - The new isolated nucleic acid molecule comprises a polynucleotide having a nucleotide sequence comprising: (a) a polynucleotide fragment of a 2475- or 3300-bp sequence or of the cDNA sequence included in ATCC Deposit No:PTA-2671, which is hybridizable to the 2475- or 3300-bp sequence, having biological activity; (b) a polynucleotide comprising nucleotides 1-2472 or 4-2472 respectively encoding amino acids 1-824 or 2-824 of the 824-amino acid sequence, without or without the start methionine; (c) a polynucleotide comprising nucleotides 1-3297 or 4-3297 respectively encoding amino acids 1-1099 or 2-1099 of the 1099-amino acid sequence, without or without the start methionine; (d) a polynucleotide encoding a polypeptide comprising 824- or 1099-amino acid sequence, or its fragment, domain or epitope; (e) a complementary sequence (antisense) to the 2475- or 3300-bp sequence; or (f) a polynucleotide capable of hybridizing under stringent conditions to (a)-(e), where the polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a sequence of only A or T residues. INDEPENDENT CLAIMS are also included for the following: (1) a recombinant vector comprising the isolated nucleic acid molecule; (2) an isolated polypeptide; (3) a recombinant host cell comprising the vector or expressing the isolated polypeptide; (4) an isolated antibody that binds specifically to the isolated polypeptide; (5) a method of producing an isolated polypeptide; (6) a method for preventing, treating or ameliorating a medical condition; (7) a method of diagnosing a pathological condition or susceptibility to a pathological condition in a subject; (8) a method for treating, or ameliorating a medical condition with the isolated polypeptide or its modulator, where the medical condition is as described in the Use section; and (9) a method of screening for candidate compounds capable of modulating the activity of a receptor polypeptide.

BIOTECHNOLOGY - Preferred Nucleic Acid: The isolated nucleic acid molecule encodes imidazoline receptor related protein. Preferred Polypeptide: The isolated polypeptide comprises: (1) a polypeptide sequence comprising 1099 amino acids, or its fragment, domain or epitope, or the encoded sequence included in ATCC Deposit No:PTA-2671, having biological activity; or (2) amino acids 1-337 or 2-337 of the 1099-amino acid sequence, respectively with or without the start methionine. Preferred Method: Diagnosing a pathological condition or susceptibility to a pathological condition in a subject comprises: (1) determining the presence or absence of a mutation in the isolated polynucleotide; and (2) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of the mutation. The method also comprises determining the presence or amount of expression of the isolated polypeptide in a biological sample and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide. The condition is as described in the Use section of this abstract. Preventing, treating or ameliorating a medical condition comprises administering to a mammalian subject the isolated polypeptide or its modulator. The modulator is a small molecule, a peptide or an antisense molecule. The modulator is an antagonist or agonist. Screening for candidate compounds capable of

modulating the activity of a receptor polypeptide comprises contacting a test compound with a cell or tissue expressing the isolated polypeptide and selecting as candidate modulating compounds those test compounds that modulate activity of the receptor polypeptide. Production (claimed): Producing the isolated polypeptide comprises culturing the recombinant host cell for expression of the polypeptide and recovering the polypeptide.

ACTIVITY - Cytostatic; Neuroprotective; Cerebroprotective; Vulnerary. No biological data given.

MECHANISM OF ACTION - None given.

USE - The nucleic acid molecule encoding imidazoline receptor related protein is useful in diagnosing, treating or preventing a medical condition, e.g., a disorder related to aberrant NF-kB activity, disorders related to aberrant NF-kB expression or activity, a disorder linked to aberrant DNA synthesis, a disorder related to aberrant imidazoline receptor activity or expression, a disorder related to aberrant kinase activity, a disorder related to aberrant serine/threonine activity, proliferative disorder associated with p21 modulation, cellular proliferation in rapidly proliferating cells, disorders in which increased number of cells in the G1 phase of the cell cycle would be therapeutically beneficial, disorders in which decreased number of cells in the G1 phase of the cell cycle would be therapeutically beneficial, disorders in which increased number of cells in the G2 phase of the cell cycle would be therapeutically beneficial, disorders in which decreased number of cells in the G2 phase of the cell cycle would be therapeutically beneficial, disorders in which decreased number of cells that progress into the S phase of the cell cycle would be therapeutically beneficial, disorders in which increased number of cells that progress into the M phase of the cell cycle would be therapeutically beneficial, disorders in which decreased number of cells that progress into the M phase of the cell cycle would be therapeutically beneficial, disorders associated with aberrant p21 activity, disorders associated with aberrant p21 expression, disorders related to aberrant signal transduction, proliferative disorder of the colon, colon cancer, colon adenocarcinoma, Peutz-Jeghers polyposis, intestinal polyps, disorders associated with the immune response to tumors, proliferative disorder of the kidney, kidney tumors, other proliferative diseases and/or disorders, male reproductive system disorders, testicular disorders, spermatogenesis disorders, infertility, Klinefelter's syndrome, XX male, epididymitis, genital warts, germinal cell aplasia, cryptorchidism, varicocele, immotile cilia syndrome, viral orchitis, proliferative disorder of the testis, testicular cancer, choriocarcinoma, Nonseminoma, seminoma, disorders of the breast, proliferative breast disorders, breast cancer, disorders of the lung, proliferative lung disorders, lung cancer, a disorder where increased NFkB expression or activity would be therapeutically beneficial, a disorder where decreased NFkB expression or activity would be therapeutically beneficial, a disorder where increased NFkB expression or activity would be therapeutically beneficial, a disorder where decreased NFkB expression or activity would be therapeutically beneficial, a disorder where increased apoptosis would be therapeutically beneficial, a disorder where decreased apoptosis would be therapeutically beneficial, healing disorder, necrosis disorder, aberrant regulation of blood pressure, feeding disorders, aberrant stimulation of locus coeruleus neurons, aberrant stimulation of insulin release, aberrant induction of the expression of glial fibrillary acidic protein independent of the action of alpha-2 adrenoceptors, dysphoric premenstrual syndrome, neurodegenerative disorders such as Alzheimer's disease, opiate addiction, monoamine turnover, nociception, aging, mood and stroke, or salivary disorders or developmental disorders (claimed).

ADMINISTRATION - Dosage comprises 1 ng to 10 mg, preferably 500 micrograms to 5 mg per kg body weight. The composition is administered via oral or parenteral route.

EXAMPLE - No relevant examples given. (115 pages)

L16 ANSWER 2 OF 4 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-20867 BIOTECHDS
TITLE: New human G-protein coupled receptor, HGPRBMY9, expressed highly in brain and testes, useful in the treatment and diagnosis of conditions such as neurodegenerative diseases, schizophrenia, lung cancer, and inflammation; a recombinant G-protein coupled receptor produced by vector-mediated gene transfer useful for disease therapy
AUTHOR: FEDER J N; MINTIER G; RAMANATHAN C S; HAWKEN D R; CACACE A M; BENNETT K L
PATENT ASSIGNEE: FEDER J N; MINTIER G; RAMANATHAN C S; HAWKEN D R; CACACE A M; BENNETT K L
PATENT INFO: US 2004147732 29 Jul 2004
APPLICATION INFO: US 2003-680402 7 Oct 2003
PRIORITY INFO: US 2003-680402 7 Oct 2003; US 2000-235709 27 Sep 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2004-561410 [54]
AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I), is new.

DETAILED DESCRIPTION - An isolated nucleic acid molecule (I) comprises a polynucleotide having a nucleotide sequence selected from: (a) a polynucleotide fragment of SEQ ID NO:1, or of the cDNA sequence included in the American Type Culture Collection Deposit Number PTA-2675 which is hybridizable to SEQ ID NO:1; (b) a polynucleotide encoding a polypeptide fragment, domain or epitope of SEQ ID NO:2 or a polypeptide fragment, domain or epitope encoded by the cDNA sequence included in ATCC Deposit No:PTA-2675; (c) a polynucleotide encoding a polypeptide of SEQ ID NO:2 or the cDNA sequence included in ATCC Deposit No:PTA-2675, which is hybridizable to SEQ ID NO: 1, and has biological activity; (d) an isolated polynucleotide comprising nucleotides 4 to 1020 of SEQ ID NO: 1, encoding a polypeptide of SEQ ID NO:2 minus the start codon; (e) a polynucleotide that represents the complementary sequence (antisense) of SEQ ID NO: 1; or (f) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(e), which does not hybridize under stringent conditions to a nucleic acid molecule comprising a nucleotide sequence of only A residues or of only T residues. INDEPENDENT CLAIMS are also included for: (1) a recombinant vector comprising the isolated nucleic acid molecule; (2) making a recombinant host cell comprising the isolated nucleic acid molecule; (3) a recombinant host cell comprising the nucleic acid molecule; (4) an isolated polypeptide (II) encoded by the nucleic acid molecule selected from: (a) a polypeptide fragment (preferably having biological activity), domain, or epitope of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No:PTA-2675; (b) a full length protein of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No:PTA-2675; (c) a polypeptide comprising amino acids 2 to 340 of SEQ ID NO:2 (i.e. the polypeptide lacking the start methionine); and (d) a polypeptide comprising amino acids 1-340 of SEQ ID NO:2; (5) an isolated antibody that binds specifically to the isolated polypeptide; (6) a recombinant host cell that expresses the isolated polypeptide; (7) a method of making an isolated polypeptide; (8) a polypeptide produced by the method; (9) preparing an isolated polypeptide from a culture of the recombinant host cell; (10) a polypeptide prepared from the recombinant host cell; (11) a method for preventing, treating, or ameliorating a medical condition by administering the polypeptide or a modulator to a mammalian subject; (12) diagnosing a (susceptibility to a) pathological condition in a subject by determining the presence or absence or a mutation in the nucleic acid molecule (I); (13) diagnosing a (susceptibility to a) pathological condition in a subject by determining the presence or amount of expression of the polypeptide; (14) screening for candidate compounds capable of modulating the activity of a G-protein coupled receptor polypeptide comprising contacting a test compound with a cell or tissue expressing the polypeptide of SEQ ID NO:2 and selecting

compounds that modulate the activity of the polypeptide as candidate therapeutics; and (15) an isolated antisense compound 8 to 30 nucleotides in length that specifically hybridizes to a nucleic acid molecule encoding the human HGPRBMY9 polypeptide, where the antisense compound inhibits the expression of the human HGPRBMY9 polypeptide.

BIOTECHNOLOGY - Preferred Molecule: The nucleic acid molecule comprises a polynucleotide fragment comprises a nucleotide sequence encoding a G-protein coupled receptor protein. Preferred Cell: The recombinant host cell comprises vector sequences.Preferred Method: The modulator of the polypeptide is a small molecule, a peptide or an antisense molecule. The modulator can be an agonist or antagonist. In screening for candidate compounds that modulating the activity of a G-protein coupled receptor the cells are CHO cells and preferably comprise a vector comprising the coding sequence of the beta lactamase gene under the control of NFAT response elements. The cells further comprise a vector comprising the coding sequence of G alpha 15 under conditions wherein G alpha 15 is expressed. The cells express the polypeptide or beta lactamase at low, moderate or high levels. Preferred Antisense Compound: The antisense compound comprises any of the sequences of SEQ ID NOs:76-136.

ACTIVITY - Analgesic; Antiaddictive; Antibacterial; Anticonvulsant; Antidepressant; Antiinflammatory; Antimanic; Antiparkinsonian; Antiserotoninergic; Cardiant; Cytostatic; Eating-Disorders-Gen.; Hemostatic; Hypnotic; Neuroleptic; Neuroprotective; Nootropic; Tranquilizer; Vasotropic; Vulnerary. No biological data given.

MECHANISM OF ACTION - G protein coupled receptor modulator.

USE - The nucleic acid molecule (I), the encoded polypeptide (II), and the associated reagents and methods are useful for diagnosing, preventing or treating conditions selected from neurodegenerative disease states, behavioral disorders, inflammatory conditions, aberrant behavior, memory disorders, aberrant cognitive functioning, dorsal raphe disorders, serotonin expression, serotonin uptake, anxiety, fear, depression, sleep disorders, pain, locus coeruleus disorders, disorders associated with a failure to maintain an attentive or alert state, nucleus accumbens disorders, disorders associated with the expression and/or release of neurotransmitters such as dopamine, opioid peptides, serotonin, GABA, and glutamate, addiction, hypothalamus disorders, disorders affecting ability of the brain to maintain homeostasis, neuroendocrine functions, hippocampus disorders, long term potentiation disorders, substantia nigra disorders, disorders affecting dopaminergic function, Alzheimer's, cognitive disorders, Parkinson's Disease, Huntington's Disease, Tourette Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, depression, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, perception, lung cancer, proliferative lung disorder, disorders associated wth aberrant E-selectin expression or activity; disorders associated wth aberrant NFkB expression or activity; disorders associated wth aberrant IkBalpha expression or activity; an inflammatory disorder; an inflammatory disorder associated with aberrant NFKB regulation or regulation of the NFkB pathway; and proliferative disorders associated with aberrant NFkB regulation or regulation of the NFkB pathway (claimed).

ADMINISTRATION - Dosage is 0.1 microgram to 1 gram. Administration is parenteral, e.g. subcutaneous, intramuscular, intravenous or intradermal; oral; topical; vaginal; or rectal.

EXAMPLE - No relevant example given. (69 pages)

L16 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-18594 BIOTECHDS
TITLE: New human G-protein coupled receptor nucleic acid for treating, e.g. a reproductive disorder, cardiovascular

disorder, pulmonary disorder, lung disorder, gastrointestinal disorder, or melanoma;
recombinant G-protein coupled receptor produced by vector-mediated gene transfer and expression in a host cell useful for disease therapy

AUTHOR: FEDER J N; MINTIER G A; RAMANATHAN C S; HAWKEN D R; CACACE A; BARBER L E; KORNACKER M G; RYSECK R; BENNETT K L; NELSON T C

PATENT ASSIGNEE: FEDER J N; MINTIER G A; RAMANATHAN C S; HAWKEN D R; CACACE A; BARBER L E; KORNACKER M G; RYSECK R; BENNETT K L; NELSON T C

PATENT INFO: US 2004121330 24 Jun 2004

APPLICATION INFO: US 2002-323412 18 Dec 2002

PRIORITY INFO: US 2002-323412 18 Dec 2002; US 2002-323412 18 Dec 2002

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2004-479663 [45]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I) encoding a human G-protein coupled receptor, is new.

DETAILED DESCRIPTION - (I) comprises a polynucleotide having a nucleotide sequence selected from: (a) a polynucleotide fragment of a sequence comprising 957 bp fully defined in the specification (SEQ ID NO. 1) or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-2682, which is hybridizable to SEQ ID NO. 1; (b) a polynucleotide encoding a polypeptide fragment of a sequence comprising 318 amino acids fully defined in the specification (SEQ ID NO. 2) or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-2682, which is hybridizable to SEQ ID NO.1; (c) a polynucleotide encoding SEQ ID NO. 2 or a polypeptide domain encoded by the cDNA sequence included in ATCC, which is hybridizable to SEQ ID NO.1; (d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO. 2 or a polypeptide epitope encoded by the cDNA sequence included in ATCC, which is hybridizable to SEQ ID NO.1; (e) a polynucleotide encoding SEQ ID NO. 2 or the cDNA sequence included in ATCC, which is hybridizable to SEQ ID NO. 1, having biological activity; (f) a polynucleotide which is a variant of SEQ ID NO.1; (g) a polynucleotide which is an allelic variant of SEQ ID NO.1; (h) a polynucleotide which encodes a species homologue of the SEQ ID NO. 2; (i) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO.1; (j) a polynucleotide corresponding to nucleotides 4-954 of SEQ ID NO.1; (k) a polynucleotide corresponding to nucleotides 1-954 of SEQ ID NO. 1; or (l) a polynucleotide capable of hybridizing to any of (a)-(k), where the polynucleotide does not hybridize to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues. INDEPENDENT CLAIMS are also included for the following: (1) a recombinant vector comprising the isolated nucleic acid molecule; (2) a method of making a recombinant host cell comprising the isolated nucleic acid molecule; (3) a recombinant host cell produced by the method of (2); (4) an isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from: (a) a polypeptide fragment of SEQ ID NO. 2 or the encoded sequence included in ATCC Deposit No: PTA-2682; (b) a polypeptide fragment of SEQ ID NO. 2 or the encoded sequence included in ATCC, having biological activity; (c) a polypeptide domain of SEQ ID NO. 2 or the encoded sequence included in ATCC; (d) a polypeptide epitope of SEQ ID NO. 2 or the encoded sequence included in ATCC; (e) a full-length protein of SEQ ID NO. 2 or the encoded sequence included in ATCC; (f) a variant of SEQ ID NO. 2; (g) an allelic variant of SEQ ID NO. 2; (h) a species homologue of SEQ ID NO. 2; (i) a polypeptide corresponding to amino acids 1-318 of SEQ ID NO. 2; or (j) a polypeptide corresponding to amino acids 2-318 of SEQ ID NO. 2; (5) an isolated antibody that binds specifically to the isolated polypeptide; (6) a recombinant host cell that expresses the isolated polypeptide; (7) a method of making an isolated polypeptide; (8) a polypeptide produced by (7); (9) a method for preventing, treating, or ameliorating a medical condition; (10) a method of diagnosing a

pathological condition or a susceptibility to a pathological condition in a subject; (11) a method for treating, or ameliorating a medical condition with the polypeptide provided as SEQ ID NO. 2, or a modulator; and (12) a method of screening for candidate compounds capable of modulating the activity of a G-protein coupled receptor polypeptide.

BIOTECHNOLOGY - Preferred Nucleic Acid: The polynucleotide fragment comprises a nucleotide sequence encoding a G-protein coupled receptor protein. The polynucleotide fragment comprises a nucleotide sequence encoding SEQ ID NO. 2 or the polypeptide encoded by the cDNA sequence included in ATCC, which is hybridizable to SEQ ID NO. 1. Preferred Host Cell: The recombinant host cell comprises the vector sequences. Preferred Method: Making an isolated polypeptide comprises culturing the recombinant host cell so that the polypeptide is expressed and recovering the polypeptide. Preventing, treating, or ameliorating a medical condition comprises administering to a mammalian subject an amount of the polypeptide or a modulator. Diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprises determining the presence or absence of a mutation in the polynucleotide and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of the mutation. Alternatively, diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprises determining the presence or amount of expression of the polypeptide in a biological sample and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide. The condition is a reproductive disorder; a male reproductive disorder; a prostate disorder; prostate cancer; proliferative condition of the prostate; cardiovascular disorder; heart disorder; pulmonary disorder; lung disorder; lung cancer; proliferative condition of the lung; gastrointestinal disorder; a colon disorder; colon cancer; female reproductive disorder; ovarian cancer; placental disorder; proliferative condition of the ovary; melanoma; vascular disorders; umbilical cord disorder; disorders associated with aberrant E-selectin expression or activity; disorders associated with aberrant NFkB expression or activity; disorders associated with aberrant IkBalpha expression or activity; an inflammatory disorder; an inflammatory disorder associated with aberrant NFkB regulation or regulation of the NFkB pathway; and a proliferative disorder associated with aberrant NFkB regulation or regulation of the NFkB pathway. The modulator is a small molecule, a peptide, or an antisense molecule. The modulator is also an antagonist or agonist. Screening for candidate compounds capable of modulating the activity of a G-protein coupled receptor polypeptide comprises: (a) contacting a test compound with a cell or tissue expressing the polypeptide comprising an amino acid sequence as set forth in SEQ ID NO. 2; and (b) selecting as candidate modulating compounds those test compounds that modulate activity of the G-protein coupled receptor polypeptide, where the candidate modulating compounds are useful for the treatment of a disorder. The cells are CHO cells. The cells comprise a vector comprising the coding sequence of the beta lactamase gene under the control of NFAT response elements. The cells further comprise a vector comprising the coding sequence of G alpha 15 under conditions where G alpha 15 is expressed. The cells express the polypeptide at low levels, at moderate levels, or at high levels, or the beta lactamase at low levels, moderate levels, or at high levels.

ACTIVITY - Gynecological; Cytostatic; Cardiovascular-Gen.; Cardiant; Respiratory-Gen.; Gastrointestinal-Gen.; Vasotropic; Antiinflammatory. No biological data given.

MECHANISM OF ACTION - Gene Therapy.

USE - The nucleic acids and polypeptides are useful for treating, e.g. reproductive disorder; a male reproductive disorder; a prostate disorder; prostate cancer; proliferative condition of the prostate; cardiovascular disorder; heart disorder; pulmonary disorder; lung disorder; lung cancer; proliferative condition of the lung; gastrointestinal disorder; a colon disorder; colon cancer; female

reproductive disorder; ovarian cancer; placental disorder; proliferative condition of the ovary; melanoma; vascular disorders; umbilical cord disorder; disorders associated with aberrant E-selectin expression or activity; disorders associated with aberrant NFkB expression or activity; disorders associated with aberrant IkBalpha expression or activity; an inflammatory disorder; an inflammatory disorder associated with aberrant NFkB regulation or regulation of the NFkB pathway; and a proliferative disorder associated with aberrant NFkB regulation or regulation of the NFkB pathway.

ADMINISTRATION - Dosage is 0.1 microg - 1 g. Administration can be oral, intravenous, intramuscular, intraarterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual, vaginal, or rectal routes.

EXAMPLE - No relevant example given. (97 pages)

L16 ANSWER 4 OF 4 BIOTECHDS COPYRIGHT 2007 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2003-13046 BIOTECHDS
TITLE: New human potassium channel beta subunit (K+betaM8) polypeptide or polynucleotide, useful for preventing, treating or ameliorating e.g. breast or colon cancer, arthritis, asthma, multiple sclerosis, osteoarthritis or ischemia;
vector-mediated gene transfer and expression in host cell for recombinant protein production for use in disease diagnosis and gene therapy
AUTHOR: FEDER J N; LEE L M; CHANG H
PATENT ASSIGNEE: BRISTOL-MYERS SQUIBB CO
PATENT INFO: WO 2003020910 13 Mar 2003
APPLICATION INFO: WO 2002-US28180 4 Sep 2002
PRIORITY INFO: US 2001-329666 16 Oct 2001; US 2001-317087 4 Sep 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-290187 [28]
AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide (designated K+betaM8), which has a potassium channel modulatory activity and which has an encoded sequence included in the American Type Culture Collection (ATCC) Deposit Number PTA-3745, is new.

DETAILED DESCRIPTION - New isolated K+betaM8 polypeptide, which has a potassium channel modulatory activity and which has an encoded sequence included in ATCC Deposit Number PTA-3745 comprises: (a) the full length protein comprising 232 amino acids (P1) fully defined in the specification; (b) a fragment, domain or epitope of P1; (c) amino acids 2-232 of P1 minus the start methionine, amino acids 1-232 of P1, amino acids 2-78 of P1 minus the start methionine, or amino acids 1-78 of P1; or (d) a polypeptide encoded by the cDNA contained in ATCC Deposit Number PTA-3745. INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule comprising: (a) a polynucleotide encoding the polypeptide cited above, which is hybridizable to a polynucleotide with a sequence having 2776 base pairs (bp) (N1) fully defined in the specification; (b) a polynucleotide fragment of N1, or a polynucleotide fragment of the cDNA sequence included in ATCC PTA-3745, which is hybridizable to N1; (c) a polynucleotide encoding the K+betaM8 polypeptide, which is encoded by the cDNA clone contained in ATCC PTA-3745; (d) nucleotides 760-1452 of N1, which encode the polypeptide with amino acids 2-232 of P1, minus the start codon; (e) nucleotides 757-1452 of N1, which encode the polypeptide corresponding to amino acids 1-232 of P1, including the start codon; (f) nucleotides 757-990 of N1, which encode the polypeptide with amino acids 1-78 of P1, including the start codon; (g) nucleotides 760-990 of N1, which encode a polypeptide with amino acids 2-78 of P1, including or minus the start codon; (h) the complementary sequence (antisense) of N1; or (i) a polynucleotide capable of hybridizing under stringent conditions to any of the above

polynucleotides, where the polynucleotide does not hybridize under stringent conditions to a nucleic acid having a nucleotide sequence of only A or T residues; (2) recombinant vectors comprising the nucleic acid; (3) recombinant host cells comprising the vector or expressing the isolated K+betaM8 polypeptide; (4) an isolated antibody that binds specifically to the K+betaM8 polypeptide; (5) a method (M1) of making an isolated polypeptide, and the polypeptide produced by the method; and (6) methods (M2) of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject.

WIDER DISCLOSURE - Also disclosed are the following: (1) a method for identifying a binding partner to the K+betaM8 polypeptide; (2) a method of identifying an activity in a biological assay; (3) a process for making polynucleotide sequences encoding a gene product having altered potassium channel modulatory activity; (4) a shuffled polynucleotide produced by a shuffling process, where the shuffled DNA encodes a gene product having enhanced tolerance to an inhibitor of the K+betaM8 polypeptide; and (5) a method of screening or identifying candidate compounds capable of binding to and/or modulating the biological activity K+betaM8.

BIOTECHNOLOGY - Preferred Polypeptide: The K+betaM8 polypeptide comprises the full length protein, where the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus. The polynucleotide fragment of the nucleic acid encoding the K+betaM8 polypeptide comprises a nucleotide sequence, which encodes a human potassium channel beta subunit. Preferred Method: In (M1), making an isolated polypeptide comprises: (a) culturing the recombinant host cell so that polypeptide is expressed; and (b) recovering the polypeptide. In (M2), diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprises: (a) determining the presence or absence of a mutation in the K+betaM8 polynucleotide; and (b) diagnosing a pathological condition or susceptibility based on the presence or absence of the mutation. The method may also comprise: (a) determining the presence or amount of expression of the K+betaM8 polypeptide in a biological sample; and (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

ACTIVITY - Cardiovascular, Vasotropic; Cardiant; Antianginal; Neuroprotective; Osteopathic; Cytostatic; Immunosuppressive; Antibacterial; Antipsoriatic; Antiinflammatory; Gynecological; Immunostimulant; Antirheumatic; Antiarthritic; Antianemic; Hemostatic; Dermatological; Antiarteriosclerotic; Virucide; Vulnerary; Antiasthmatic. Test details are described but no results are given.

MECHANISM OF ACTION - Potassium Channel Modulator; Gene Therapy.

USE - The K+betaM8 polypeptide or polynucleotide is useful for preventing, treating or ameliorating a medical condition, particularly a male reproductive disorder, a testicular disorder; testicular cancer; a neural disorder, a disorder related to aberrant calcium regulation, a disorder related to aberrant potassium regulation, a disorder related to aberrant potassium channel regulation, a pulmonary disorder, immune system disorders, female reproductive disorders, breast cancer, colon cancer, a disorder associated with mis-regulation of NFkB, an inflammatory disorder, an innate immunity disorder, a disorder associated with a failure to initiate and/or sustain an adequate inflammatory response, rheumatoid arthritis, asthma, multiple sclerosis, osteoarthritis, a T-cell mediated autoimmune disease, or psoriasis (all claimed). The polynucleotide or polypeptide is particularly useful in gene therapy for treating these conditions, or for treating e.g. anemia, thrombocytopenia, systemic lupus erythematosus, congestive heart failure, pulmonary heart disease, angina pectoris, coronary arteriosclerosis, aneurysms, ischemia, Kaposi's sarcoma, Crohn's disease, infections (e.g. viral or bacterial) or wounds. The K+betaM8 polypeptide or polynucleotide is also useful for diagnosing the above-mentioned pathological conditions, or a susceptibility to these conditions. The polypeptide or

polynucleotide may be used in animals e.g. cows, pigs, chickens, cats and dogs) or humans.

ADMINISTRATION - Dosage is 1.0 microg/kg/day - 10 mg/kg/day, preferably 0.01-1 mg/kg/day. Administration is intravenous, topical, intradermal, intramuscular, intraperitoneal, subcutaneous, intranasal, epidural or oral.

EXAMPLE - Experimental protocols are described but no results are given. (308 pages)

```
=> d his

     (FILE 'HOME' ENTERED AT 15:00:23 ON 29 JAN 2007)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 15:00:55 ON 29 JAN 2007
L1          3538 S BCL-6
L2          3466 S "NFKB"
L3             0 S L1 AND L2
L4           265 S LAZ3 OR "ZINC FINGER PROTEIN 51"
L5             0 S L2 AND L4
L6         49561 S "B CELL CLL" OR "B CELL LYMPHOMA"
L7            24 S L6 AND L2
L8            22 DUP REM L7 (2 DUPLICATES REMOVED)
                 E NADLER S G/AU
L9           177 S E3
                 E NEUBAUER M G/AU
L10           74 S E3
                 E FEDER J N/AU
L11          190 S E3
                 E CARMAN J/AU
L12          105 S E3
L13          538 S L9 OR L10 OR L11 OR L12
L14            0 S L13 AND L8
L15            4 S L13 AND L2
L16            4 DUP REM L15 (0 DUPLICATES REMOVED)
```

	Issue Date	Pages	Document ID	Title
1	20051020	33	US 20050233367 A1	Device for extracting biological molecules from tissue specimens and methods for preparing the same
2	20050609	201	US 20050123912 A1	Nucleic-acid associated proteins
3	20050414	27	US 20050079492 A1	Micro-arrayed organization of transcription factor target genes
4	20040902	125	US 20040171823 A1	Polynucleotides and polypeptides associated with the NF-kappaB pathway

	L #	Hits	Search Text
1	L1	140	BCL-6
2	L2	1800	NFkB
3	L3	3	l1 and l2
4	L4	1789557	inhibit$3 or decrease$3
5	L5	133	l1 and l4
6	L6	3	l2 and l5
7	L7	10265	FEDER CARMAN NADLER NEUBAUER
8	L8	4	l1 and l7

	Issue Date	Pages	Document ID	Title
1	20070118	54	US 20070015250 A1	Methods and compositions for increasing longevity and protein yield from a cell culture
2	20070104	33	US 20070003515 A1	Method of inducing memory b cell development and terminal differentiation
3	20061228	33	US 20060292560 A1	Transcription factor target gene discovery
4	20061207	60	US 20060275294 A1	METHOD OF PREVENTION AND TREATMENT OF AGING, AGE-RELATED DISORDERS AND/OR AGE-RELATED MANIFESTATIONS INCLUDING ATHEROSCLEROSIS, PERIPHERAL VASCULAR DISEASE, CORONARY ARTERY DISEASE, OSTEOPOROSIS, ARTHRITIS, TYPE 2 DIABETES, DEMENTIA, ALZHEIMERS DISEASE AND CANCER
5	20061116	27	US 20060257948 A1	Antibody tools for the diagnostic use in the medical therapy with inhibitors of histone deacetylases
6	20061102	44	US 20060247305 A1	Chromen-4-one inhibitors of anti-apoptotic Bcl-2 family members and the uses thereof
7	20061026	79	US 20060241157 A1	Heterocyclic ppar modulators
8	20060928	115	US 20060216706 A1	Proteins associated with cell growth, differentiation, and death

	Issue Date	Pages	Document ID	Title
9	20060921	39	US 20060211112 A1	Growth of human dendritic cells for cancer immunotherapy in closed system using microcarrier beads
10	20060810	30	US 20060178435 A1	Apogossypolone and the uses thereof
11	20060720	46	US 20060160897 A1	Topical Use of Valproic Acid for the Prevention or Treatment of Skin Disorders
12	20060713	19	US 20060153820 A1	Materials and methods relating to the production and maintenance of cell lines
13	20060629	150	US 20060141493 A1	Atherosclerotic phenotype determinative genes and methods for using the same
14	20060622	28	US 20060136142 A1	Systems, methods and computer program products for guiding selection of a therapeutic treatment regimen based on the methylation status of the DNA
15	20060615	173	US 20060127894 A1	Protein associated with cell growth, differentiation, and death
16	20060608	23	US 20060121483 A1	Methods for detecting teneurin signalling and related screening methods
17	20060525	49	US 20060110793 A1	Methods and compositions for increasing longevity and protein yield from a cell culture

	Issue Date	Pages	Document ID	Title
18	20060525	34	US 20060110735 A1	Use of molecular markers for the preclinical and clinical profiling of inhibitors of enzymes having histone deacetylase activity
19	20060518	195	US 20060105376 A1	Novel full-length cDNA
20	20060511	46	US 20060099613 A1	Use of antisense oligonucleotide libraries for identifying gene function
21	20060420	131	US 20060084647 A1	Small molecule inhibitors of anti-apoptotic BCL-2 family members and the uses thereof
22	20060413	28	US 20060080745 A1	Gene reactivation by somatic hypermutation
23	20060406	131	US 20060074023 A1	Angiogenesis associated proteins, and nucleic acids encoding the same
24	20060323	51	US 20060063231 A1	Compositions and methods for protein production
25	20060316	52	US 20060057123 A1	Method of inducing memory B cell development and terminal differentiation
26	20060216	83	US 20060035344 A1	Double-stranded rna structures and constructs, and methods for generating and using the same

	Issue Date	Pages	Document ID	Title
27	20060209	28	US 20060029574 A1	Biomarkers for diagnosis, prognosis, monitoring, and treatment decisions for drug resistance and sensitivity
28	20060202	47	US 20060024268 A1	Modulation of immunoglobulin production and atopic disorders
29	20060126	142	US 20060019310 A1	Cell regulatory genes, encoded products, and uses related thereto
30	20051229	112	US 20050287648 A1	Protein Transducing Domain/Deaminase Chimeric Proteins, Related Compounds, and Uses Thereof
31	20051215	29	US 20050277583 A1	Histone deacetylase inhibitors and process for producing the same
32	20051208	154	US 20050272055 A1	Method of treating lethal shock induced by toxic agents and diagnosing exposure to toxic agents by measuring distinct pattern in the levels of expression of specific genes
33	20051117	15	US 20050255443 A1	Method of screening cell growth inhibitor and cell growth inhibitor
34	20051027	74	US 20050239728 A1	Double stranded rna structures and constructs, and methods for generating and using the same
35	20051020	21	US 20050234135 A1	Gossypol co-crystals and the use thereof

	Issue Date	Pages	Document ID	Title
36	20051020	33	US 20050233367 A1	Device for extracting biological molecules from tissue specimens and methods for preparing the same
37	20051013	23	US 20050229272 A1	Compositions and methods for gene silencing
38	20051006	59	US 20050222012 A1	Methods and compositions for treating leukemia
39	20050929	30	US 20050215501 A1	Methods and products for enhancing epitope spreading
40	20050922	114	US 20050208529 A1	Methods and compositions for immuno-histochemical detection
41	20050811	18	US 20050176686 A1	Novel compounds as histone deacetylase inhibitors
42	20050804	45	US 20050170359 A1	Treatment of vascular dysfunction and alzheimer's disease
43	20050728	17	US 20050164272 A1	Genes differentially expressed in secretory versus proliferative endometrium
44	20050721	148	US 20050158737 A1	Tumour associated antigens
45	20050630	45	US 20050142105 A1	Chimeric molecule for the treatment of th2-like cytokine mediated disorders
46	20050616	49	US 20050130146 A1	Histone deacetylase 9
47	20050609	201	US 20050123912 A1	Nucleic-acid associated proteins

48	20050602	177	US 20050118582 A1	Nucleic acid-associated proteins

	Issue Date	Pages	Document ID	Title
49	20050505	29	US 20050095712 A1	Mutations caused by activation-induced cytidine deaminase
50	20050421	47	US 20050084490 A1	Boroproline compound combination therapy
51	20050414	33	US 20050079513 A1	Classification of patients having diffuse large B-cell lymphoma based upon gene expression
52	20050414	27	US 20050079492 A1	Micro-arrayed organization of transcription factor target genes
53	20050331	104	US 20050069878 A1	Proteins associated with cell growth, differentiation, and death
54	20050324	379	US 20050064458 A1	143 human secreted proteins
55	20050303	232	US 20050048490 A1	Proteins associated with cell growth, differentiation, and death
56	20050303	8	US 20050048051 A1	Method for controlled induction of somatic mutations and use thereof in proteomics
57	20050217	50	US 20050038113 A1	Valproic acid and derivatives for the combinatorial therapeutic treatment of human cancers and for the treatment of tumor metastasis and minimal residual disease
58	20050210	88	US 20050032794 A1	Diamine derivatives of quinone and uses thereof

	Issue Date	Pages	Document ID	Title
59	20050127	29	US 20050021240 A1	Systems, methods and computer program products for guiding selection of a therapeutic treatment regimen based on the methylation status of the DNA
60	20041125	24	US 20040234965 A1	Novel pathways involved in epigenetic memory
61	20041028	143	US 20040214902 A1	Small molecule antagonists of BCL-2 family proteins
62	20040902	125	US 20040171823 A1	Polynucleotides and polypeptides associated with the NF-kappaB pathway
63	20040902	166	US 20040171012 A1	Nucleic acid-associated proteins
64	20040805	152	US 20040152877 A1	Nucleic acid-associated proteins
65	20040729	115	US 20040146970 A1	Proteins associated with cell growth, differentiation, and death
66	20040729	58	US 20040146879 A1	Novel human genes and gene expression products
67	20040722	30	US 20040141982 A1	Use of genetically engineered antibodies to treat multiple myeloma
68	20040715	60	US 20040137448 A1	Nucleic acid-associated proteins
69	20040708	128	US 20040132120 A1	Cell regulatory genes, encoded products, and uses related thereto

70	20040708	199	US 20040132086 A1	Progesterone receptor-regulated gene expression and methods related thereto

	Issue Date	Pages	Document ID	Title
71	20040708	140	US 20040132043 A1	Proteins Associated with cell growth, differentiation, and death
72	20040624	94	US 20040121361 A1	Nucleic acid-associated proteins
73	20040527	154	US 20040101884 A1	Molecules for disease detection and treatment
74	20040506	24	US 20040087652 A1	Valproic acid and derivatives thereof as histone deacetylase inhibitors
75	20040422	62	US 20040077601 A1	Methods and compositions relating to isoleucine boroproline compounds
76	20040415	58	US 20040072769 A1	Methods for design and selection of short double-stranded oligonucleotides, and compounds of gene drugs
77	20040318	65	US 20040053291 A1	Nucleic acid-associated proteins
78	20040226	259	US 20040038207 A1	Gene expression in bladder tumors
79	20040212	76	US 20040029144 A1	Transcription factors and zinc finger proteins
80	20040129	84	US 20040018522 A1	Identification of dysregulated genes in patients with multiple sclerosis
81	20040108	165	US 20040005560 A1	Novel full-length cDNA

	Issue Date	Pages	Document ID	Title
82	20031225	36	US 20030235813 A1	In vivo assay and molecular markers for testing the phenotypic stability of cell populations, and selecting cell populations for autologous transplantation
83	20031204	161	US 20030224993 A1	Compositions that inhibit proliferation of cancer cells
84	20031127	65	US 20030219740 A1	DNA sequences isolated from human colonic epithelial cells
85	20031113	58	US 20030211513 A1	Intracellular signaling proteins
86	20031030	32	US 20030203416 A1	ZAP-70 expression as a marker for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
87	20031023	139	US 20030198975 A1	Proteins associated with cell growth, differentiation, and death
88	20031009	42	US 20030190640 A1	Genes expressed in prostate cancer
89	20030925	35	US 20030180799 A1	Antibodies against plasma cells
90	20030807	13	US 20030148326 A1	Diagnosis of diseases associated with dna transcription
91	20030731	45	US 20030143712 A1	Histone deacetylase and methods of use thereof
92	20030724	75	US 20030139330 A1	Transcription factors containing two potential dna binding motifs

	Issue Date	Pages	Document ID	Title
93	20030605	54	US 20030104393 A1	Blood assessment of injury
94	20030522	274	US 20030097666 A1	Novel human genes and gene expression products:II
95	20030501	59	US 20030082620 A1	Novel human genes and gene expression products: II
96	20030417	87	US 20030073613 A1	Angiogenisis associated proteins, and nucleic acids encoding the same
97	20030320	46	US 20030054354 A1	Use of antisense oligonucleotide libraries for identifying gene function
98	20030220	31	US 20030036070 A1	Gene expression profiling of inflammatory bowel disease
99	20030206	401	US 20030027999 A1	143 human secreted proteins
100	20030206	46	US 20030027208 A1	Progesterone receptor-regulated gene expression and methods related thereto
101	20030116	37	US 20030012776 A1	Nucleic acid and protein expressed thereby and their involvement in stress
102	20030109	49	US 20030008924 A1	Small molecule antagonists of Bcl-2 family proteins
103	20021128	30	US 20020177218 A1	Methods of detecting multiple DNA binding protein and DNA interactions in a sample, and devices, systems and kits for practicing the same

	Issue Date	Pages	Document ID	Title
104	20021128	19	US 20020177149 A1	Systems and methods for automated analysis of cells and tissues
105	20020912	68	US 20020127615 A1	TRAF-3 deletion isoforms and uses thereof
106	20020328	70	US 20020037538 A1	Compositions, kits, and methods for identification, assessment, prevention, and therapy of psoriasis
107	20020321	50	US 20020034758 A1	Novel human genes and gene expressions products: II
108	20011122	16	US 20010044104 A1	Genes defferentially expressed in secretory versus proliferative endometrium
109	20011018	20	US 20010031261 A1	Use of genetically engineered antibodies to treat multiple myeloma
110	20010809	56	US 20010012887 A1	Cloning and uses of the genetic locus bcl-6
111	20010802	75	US 20010010922 A1	CLONING AND USES OF THE GENETIC LOCUS BCL-6
112	20061212	45	US 7148257 B2	Methods of treating mesothelioma with suberoylanilide hydroxamic acid
113	20061010	234	US 7119173 B2	Secreted and transmembrane polypeptides and nucleic acids encoding the same
114	20061010	398	US 7118887 B2	Nucleic acid overexpressed in esophageal tumor, normal stomach and melanoma

	Issue Date	Pages	Document ID	Title
115	20060912	129	US 7105149 B1	Isolation of five novel genes coding for new Fc receptors-type melanoma involved in the pathogenesis of lymphoma/myeloma
116	20060418	129	US 7030227 B1	Cell regulatory genes, encoded products, and uses related thereto
117	20060228	60	US 7005499 B1	Wnt-regulated cytokine-like polypeptide and nucleic acids encoding same
118	20050920	139	US 6946256 B1	Cell regulatory genes, encoded products, and uses related thereto
119	20050830	247	US 6936417 B2	Gene expression in bladder tumors
120	20050426	15	US 6884578 B2	Genes differentially expressed in secretory versus proliferative endometrium
121	20050201	67	US 6849415 B2	TRAF-3 deletion isoforms and uses thereof
122	20040831	53	US 6783945 B2	Cloning and uses of the genetic locus bcl-6
123	20040615	187	US 6750015 B2	Progesterone receptor-regulated gene expression and methods related thereto
124	20040106	38	US 6673587 B1	Histone deacetylase, and uses therefor
125	20020625	56	US 6410710 B1	Nucleic acid encoding a TRAF-3 deletion isoform
126	20020101	227	US 6335170 B1	Gene expression in bladder tumors

127	20010717	45	US 6262116 B1	Transcription therapy for cancers

	Issue Date	Pages	Document ID	Title
128	20010508	27	US 6228645 B1	Promoter elements conferring root-preferred gene expression
129	20010116	61	US 6174997 B1	Cloning and uses of the genetic locus BCL-6
130	20001031	44	US 6140125 A	Antisense inhibition of bcl-6 expression
131	20000215	62	US 6025194 A	Nucleic acid sequence of senescence asssociated gene
132	19990706	35	US 5919997 A	Transgenic mice having modified cell-cycle regulation
133	19990316	52	US 5882858 A	Cloning and uses of the genetic locus BCL-6